```
=> FILE HCAPLUS
FILE 'HCAPLUS' ENTERED AT 17:55:39 ON 14 MAY 1997
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FILE COVERS 1967 - 14 May 1997 VOL 126 ISS 21
FILE LAST UPDATED: 14 May 1997 (970514/ED)

 To help control your online searching costs, consider using the
 HCAplus file when using the FSEARCH command or when conducting
 SmartSELECT searches with large numbers of terms.

 Some chemical substances have deleted CAS Registry Numbers. To
 ensure that you are using the most current CAS Registry Number,
 and for a more complete search, start your CAS Registry Number
 search in the REGISTRY file. Then use the L-number answer set
 from REGISTRY as a search term in HCAplus.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> D QUE L34
L10          3239 SEA FILE=HCAPLUS ABB=ON  CHIMER?(4A)PROTEIN#
L11         21374 SEA FILE=HCAPLUS ABB=ON  TRANSCRIPTION(2A)FACTOR#
L12           214 SEA FILE=HCAPLUS ABB=ON  L10 AND L11
L13         15077 SEA FILE=HCAPLUS ABB=ON  (2 OR 3 OR TWO OR THREE OR SECON
                 D OR THIRD)(2A)DOMAIN#
L14            22 SEA FILE=HCAPLUS ABB=ON  L12 AND L13
L17          2787 SEA FILE=HCAPLUS ABB=ON  (ZINC OR ZN)(W)FINGER#
L18            26 SEA FILE=HCAPLUS ABB=ON  L12 AND L17
L20          1062 SEA FILE=HCAPLUS ABB=ON  (FUSION/IT(L)CHIMER?/IT(L)PROTEI
                 N#/IT)
L21            52 SEA FILE=HCAPLUS ABB=ON  L11 AND L20
L22           169 SEA FILE=HCAPLUS ABB=ON  L20(L)(PREP OR SPN)/RL
L23             6 SEA FILE=HCAPLUS ABB=ON  L21 AND L22
L24             3 SEA FILE=HCAPLUS ABB=ON  (L14 OR L18) AND L22
L25             1 SEA FILE=HCAPLUS ABB=ON  L14 AND L20
L26             5 SEA FILE=HCAPLUS ABB=ON  L18 AND L20
L27         10727 SEA FILE=HCAPLUS ABB=ON  GENE(W)THERAPY OR GENETIC(W)ENGI
                 NEERING
L28            20 SEA FILE=HCAPLUS ABB=ON  L22 AND L27
L29            10 SEA FILE=HCAPLUS ABB=ON  L23 OR L24 OR L25 OR L26
L31             2 SEA FILE=HCAPLUS ABB=ON  L28 AND TRANSCRIPTION
L32            10 SEA FILE=HCAPLUS ABB=ON  L29 OR L31
L33             8 SEA FILE=HCAPLUS ABB=ON  L12 AND L27
L34            15 SEA FILE=HCAPLUS ABB=ON  L32 OR L33

=> FILE WPIDS
FILE 'WPIDS' ENTERED AT 17:55:50 ON 14 MAY 1997
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FILE LAST UPDATED: 12 MAY 97                <97.512/UP>
<<<UPDATE WEEKS:
MOST RECENT DERWENT WEEK             9719   <19?719 DW>
DERWENT WEEK FOR CHEMICAL CODING:    9711
DERWENT WEEK FOR POLYMER INDEXING:   9716
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
<<< D COST AND SET NOTICE DO NOT REFLECT SUBSCRIBER DISCOUNTS -
                                SEE HELP COST FOR DETAILS <<<
<<< PCT PUBLICATIONS FROM 19 DECEMBER 1996  - SEE NEWS <<<

=> D QUE L42
L36            17 SEA FILE=WPIDS ABB=ON  CHIMAER. 3A PROTEIN#
L37          2949 SEA FILE=WPIDS ABB=ON  TRANSCRIPTION
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L38             2 SEA FILE=WPIDS ABB=ON  L36 AND L37
L39             1 SEA FILE=WPIDS ABB=ON  CHIMAER? 4A TRANSCRIPTION W FACTOR
                  #
L40           946 SEA FILE=WPIDS ABB=ON  GENE(W)THERAPY
L41             2 SEA FILE=WPIDS ABB=ON  L38 AND L40
L42             2 SEA FILE=WPIDS ABB=ON  L39 OR L39 OR L41

=> FILE BIOSIS
FILE 'BIOSIS' ENTERED AT 17:56:02 ON 14 MAY 1997
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 May 1997 (9705l2/ED
CAS REGISTRY NUMBERS (R) LAST ADDED: 12 May 1997 (970512/UP)


=> D QUE L43
L43          2019 SEA FILE=BIOSIS ABB=ON  CHIMER(4A)PROTEIN#
L44         37610 SEA FILE=BIOSIS ABB=ON  TRANSCRIPTION
L45           293 SEA FILE=BIOSIS ABB=ON  L43 AND L44
L46            22 SEA FILE=BIOSIS ABB=ON  L45 AND (2 OR 3 OR SECOND OR THIR
                  D OR TWO OR THREE)(2A)DOMAIN#
L47           199 SEA FILE=BIOSIS ABB=ON  L45 AND (BIND? OR FUSION)
L48            20 SEA FILE=BIOSIS ABB=ON  L46 AND L47
L49             3 SEA FILE=BIOSIS ABB=ON  (ZN OR ZINC) AND  L48
L50          1232 SEA FILE=BIOSIS ABB=ON  HOMEODOMAIN?
L51             1 SEA FILE=BIOSIS ABB=ON  L50 AND L48
L52            12 SEA FILE=BIOSIS ABB=ON  L45 AND L50
L53            14 SEA FILE=BIOSIS ABB=ON  L49 OR L51 OR L52
L54             2 SEA FILE=BIOSIS ABB=ON  L45 AND GENE(W)THERAPY
L55            16 SEA FILE=BIOSIS ABB=ON  L53 OR L54

=> FILE MEDLINE
FILE 'MEDLINE' ENTERED AT 17:56:13 ON 14 MAY 1997

 FILE LAST UPDATED: 7 MAY 1997 (19970507/UP).  FILE COVERS 1966 TO DATE.
 +QLF/CT SHOWS YOU THE ALLOWABLE QUALIFIERS OF A TERM.

 MEDLINE, CANCERLIT AND PDQ ERRONEOUSLY ANNOTATED CERTAIN ARTICLES
 AUTHORED OF CO-AUTHORED BY DR. BERNARD FISHER WITH THE PHRASE
 "SCIENTIFIC MISCONDUCT-DATA TO BE REANALYZED."  ALL SUCH ANNOTATIONS
 HAVE BEEN REMOVED OR ARE BEING REMOVED.  WE APOLOGIZE FOR ANY PROBLEMS
 OR CONCERNS THIS MAY HAVE CAUSED.  USERS SHOULD DISREGARD THOSE PRIOR
 ANNOTATIONS.

 MEDLINE ANNUAL RELOAD AVAILABLE ON STN IN RECORD TIME (2/08/97).
 ENTER HELP RLOAD FOR DETAILS.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> D QUE L67
L43          2019 SEA FILE=BIOSIS ABB=ON  CHIMER(4A)PROTEIN#
L44         37610 SEA FILE=BIOSIS ABB=ON  TRANSCRIPTION
L45           293 SEA FILE=BIOSIS ABB=ON  L43 AND L44
L46            22 SEA FILE=BIOSIS ABB=ON  L45 AND (2 OR 3 OR SECOND OR THIR
                  D OR TWO OR THREE)(2A)DOMAIN#
L47           199 SEA FILE=BIOSIS ABB=ON  L45 AND (BIND? OR FUSION)
L48            21 SEA FILE=BIOSIS ABB=ON  L46 AND L47
L49             3 SEA FILE=BIOSIS ABB=ON  (ZN OR ZINC) AND  L48
L50          1232 SEA FILE=BIOSIS ABB=ON  HOMEODOMAIN?
L51             1 SEA FILE=BIOSIS ABB=ON  L50 AND L48
```

```
L52          12 SEA FILE=BIOSIS ABB=ON  L48 AND L51
L53          14 SEA FILE=BIOSIS ABB=ON  L49 OR L51 OR L52
L54           2 SEA FILE=BIOSIS ABB=ON  L48 AND GENE W THERAPY
L56          47 SEA FILE=MEDLINE ABB=ON  L53 OR L54
L57        2741 SEA FILE=MEDLINE ABB=ON  CHIMERIC PROTEINS+NT/CT
L58         963 SEA FILE=MEDLINE ABB=ON  HOMEODOMAIN PROTEINS+NT/CT
L59          13 SEA FILE=MEDLINE ABB=ON  L56 AND L57 AND L58
L61       17592 SEA FILE=MEDLINE ABB=ON  RECOMBINANT FUSION PROTEINS+NT C
                T
L62          36 SEA FILE=MEDLINE ABB=ON  L56 AND L61
L63          31 SEA FILE=MEDLINE ABB=ON  L62 AND (L57 OR L58)
L64       55835 SEA FILE=MEDLINE ABB=ON  TRANSCRIPTION FACTORS+NT/CT
L65          21 SEA FILE=MEDLINE ABB=ON  L63 AND L64
L66          12 SEA FILE=MEDLINE ABB=ON  L59 AND L65
L67          21 SEA FILE=MEDLINE ABB=ON  L65 OR L66

=> DUP REM L34 L42 L55 L67
FILE 'HCAPLUS' ENTERED AT 17:56:31 ON 14 MAY 1997
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FILE 'BIOSIS' ENTERED AT 17:56:31 ON 14 MAY 1997
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FILE 'MEDLINE' ENTERED AT 17:56:31 ON 14 MAY 1997
PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L42
PROCESSING COMPLETED FOR L55
PROCESSING COMPLETED FOR L67
L68          47 DUP REM L34 L42 L55 L67 (7 DUPLICATES REMOVED)

=> D L68 ALL 1-47

L68  ANSWER 1 OF 47  HCAPLUS  COPYRIGHT 1997 ACS
AN   1996:759342  HCAPLUS
DN   126:43287
TI   Tethering human immunodeficiency virus type 1 preintegration
     complexes to target DNA promotes integration at nearby sites
AU   Bushman, Frederic D.; Miller, Michael D.
CS   Infectious Disease Lab., Salk Inst. Biol. Studies, La Jolla, CA,
     92037, USA
SO   J. Virol. (1997), 71(1), 458-464
     CODEN: JOVIAM; ISSN: 0022-538X
DT   Journal
LA   English
CC   3-2 (Biochemical Genetics)
     Section cross-reference(s): 10
AB   Integration of retroviral cDNA in vivo is normally not sequence
     specific with respect to the integration target DNA.  We have been
     investigating methods for directing the integration of retroviral
     DNA to predetd. sites, with the dual goal of understanding potential
     mechanisms governing normal site selection and developing possible
     methods for gene therapy.  To this end, we have
     fused retroviral integrase enzymes to sequence-specific DNA-binding
     domains and investigated target site selection by the resulting
     proteins.  In a previous study, we purified and analyzed a fusion
     protein composed of human immunodeficiency virus integrase linked to
     the DNA-binding domain of .lambda. repressor.  This fusion could
     direct selective integration in vitro into target DNA contg.
     .lambda. repressor binding sites.  Here we investigate the
     properties of a fusion integrase in the context of a human
```

immunodeficiency virus provirus. We used a fusion of integrase to the DNA binding domain of the **zinc finger** protein zif268 (IN-zif). Initially we found that the fusion was highly detrimental to replication as measured by the multinuclear activation of a galactosidase indicator (MAGI) assay for infected centers. However, we found that viruses contg. mixts. of wild-type integrase and IN-zif were infectious. We prepd. preintegration complexes from cells infected with these viruses and found that such complexes directed increased integration near zif268 recognition sites.

ST HIV1 preintegration complex tethering DNA integration

IT DNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(-binding domain, fusion of integrase to the DNA binding domain of the **zinc finger** protein zif268; tethering HIV-1 preintegration complexes to target DNA promotes integration at nearby sites)

IT **Gene therapy**
(directing the integration of retroviral DNA to predetd. sites, with the dual goal of understanding potential mechanisms governing normal site selection and developing possible methods for **gene therapy**)

IT **Fusion proteins** (**chimeric proteins**)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fused HIV-1 retroviral integrase enzymes to sequence-specific DNA-binding domains and investigated target site selection by the resulting **proteins**)

IT DNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(target; tethering HIV-1 preintegration complexes to target DNA promotes integration at nearby sites)

IT Human immunodeficiency virus 1
Integration (genetic)
(tethering HIV-1 preintegration complexes to target DNA promotes integration at nearby sites)

IT Genetic elements
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**transcription factor** zif268-responsive element; preintegration complexes from cells infected with HIV-1 contg. mixts. of wild-type integrase and IN-zif directed increased integration near zif268 recognition sites)

IT **Transcription factors**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(zif268, fusion of integrase to the DNA binding domain of the **zinc finger** protein zif268; tethering HIV-1 preintegration complexes to target DNA promotes integration at nearby sites)

IT 52359-99-3, Integrase
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(retroviral; fused HIV-1 retroviral integrase enzymes to sequence-specific DNA-binding domains and investigated target site selection by the resulting proteins)

L68 ANSWER 2 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 97:118939 BIOSIS
DN 99425441
TI Decoy approach using RNA-DNA chimera oligonucleotides to inhibit the

regulatory function of human immunodeficiency virus type 1 Rev protein.

AU Nakaya T; Iwai S; Fujinaga K; Sato Y; Otsuka E; Ikuta K
CS Section Serol., Inst. Immunol. Sci., Hokkaido Univ., Kita-15, Nishi-7, Kita-ku, Sapporo 060, Japan
SO Antimicrobial Agents and Chemotherapy 41 (2). 1997. 319-325. ISSN: 0066-4804
LA English
PR Biological Abstracts Vol. 103 Iss. 007 Ref. 097584
AB Human immunodeficiency virus type 1 (HIV-1) encodes two regulatory proteins, Tat and Rev, that bind to target RNA sequences. These are the trans-activation responsive (TAR) RNA and the Rev-responsive element (RRE), respectively. The Rev protein shifts RNA synthesis to viral late transcripts by binding to the RRE within the env gene. In the present study we prepared a RNA-DNA chimera consisting of 29 or 31 nucleotides to inhibit the Rev regulatory function by means of the decoy approach. The chimera oligonucleotides (anti-Rev oligonucleotides (AROs)) contained an RNA "bubble" structure (13 oligonucleotides; the Rev-binding element in RRE) that bound Rev with a high affinity in an in vitro assay. The controls were RNA-DNA chimera oligonucleotides (negative control oligonucleotides (NCOs)) similar to ARO, but without the bubble structure, that bound with considerably less affinity to Rev. When the inhibitory effects of these decoys on HIV-1 replication were examined, we found that AROs, but not NCOs, reduced more than 90% of the HIV-1 production generated by productively infected human T-cell lines. The production of primary HIV-1 isolates in healthy donor-derived peripheral blood mononuclear cells was also similarly inhibited by AROs. In addition, the induction of viral mRNAs and antigens in latently HIV-1-infected ACH-2 cells by tumor necrosis factor alpha was specifically inhibited by AROs, but not by NCOs. No apparent cytotoxicity was caused by either decoy. Thus, the use of a Rev-binding element-based decoy, the RNA-DNA chimera oligonucleotide, may represent a safer approach to **gene therapy** for reducing the virus load in HIV-1-infected individuals.
ST RESEARCH ARTICLE; HUMAN IMMUNODEFICIENCY VIRUS TYPE 1; HUMAN; PATHOGEN; HOST; HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 REV **PROTEIN**; RNA-DNA **CHIMERA** OLIGONUCLEOTIDES; **TRANSCRIPTION**; INFECTION; **GENE THERAPY**; THERAPEUTIC METHOD
CC Pathology, General and Miscellaneous-Therapy *12512
Genetics of Bacteria and Viruses *31500
Virology-Animal Host Viruses 33506
Medical and Clinical Microbiology-Virology *36006
BC Retroviridae 02623
Hominidae 86215

L68 ANSWER 3 OF 47 MEDLINE
AN 97188596 MEDLINE
TI Mapping of a potent transcriptional repression region of the human **homeodomain** protein EVX1.
AU Briata P; Ilengo C; Van DeWerken R; Corte G
CS Laboratory of Immunobiology I.S.T., Advanced Biotechnology Center, Genova, Italy.. briata@sirio.cba.unige.it
SO FEBS LETTERS, (1997 Feb 3) 402 (2-3) 131-5.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9705
EW 19970504
AB The human **homeodomain** protein EVX1 is a transcriptional repressor in transfected mammalian cells and this function depends on a region carboxyl-terminal to the **homeodomain**. In this

study, we transiently expressed several deletions of the EVX1 C-terminal region in mammalian cells and investigated their effect on the **transcription** of a reporter gene directed by different promoters. We show that the repressor activity maps to a region of 31 amino acids with a high abundance of alanine and proline residues. This region is able to transfer the repressor function to either the entire HOX06 or CREB **transcription** factors, or to the GAL4 DNA binding domain.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Cell Line
Chimeric Proteins: CH, chemistry
Chimeric Proteins: ME, metabolism
Glucagonoma
Hamsters
***Homeodomain Proteins: CH, chemistry**
***Homeodomain Proteins: ME, metabolism**
Insulinoma
Mice
Molecular Sequence Data
Mutagenesis, Site-Directed
Pancreatic Neoplasms
Polymerase Chain Reaction
Repressor Proteins: CH, chemistry
Repressor Proteins: ME, metabolism
Sequence Deletion
Transcription, Genetic
Transfection
Tumor Cells, Cultured
3T3 Cells

RN 130173-73-9 (Evx-1 protein)
CN 0 (**Chimeric Proteins**); 0 (**Homeodomain** Proteins); 0 (Repressor Proteins)

L68 ANSWER 4 OF 47 HCAPLUS COPYRIGHT 1997 ACS DUPLICATE 1
AN 1996:537731 HCAPLUS
DN 125:160379
TI DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing fusion products
IN Pomerantz, Joel L.; Sharp, Phillip A.; Pabo, Carl O.
PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
PI WO 9620951 A1 960711
DS W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-US16992 951229
PRAI US 94-366083 941229
DT Patent
LA English
IC ICM C07K014-00
ICS C12N015-00; C12P021-00; A61K067-00
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 13
AB **Chimeric proteins** contg. composite DNA-binding regions are disclosed together with DNA constructs encoding them, compns. contg. them and applications in which they are useful. **Zinc finger** domains and homeodomains in fusion products are useful **transcription factors** for RNA DNA recognition or gene regulation. FK1012 dimerization and

gene therapy are included.

ST **transcription factor** chimeric **gene**
therapy recognition; DNA binding **protein**
chimera gene therapy; homeodomain
zinc finger chimeric **transcription**
factor

IT **Genetic engineering**
Molecular cloning
(DNA-binding **protein chimeric** gene
constructs, expression in eukaryote cell and animal, and
zinc finger- and homeodomain-contg.
fusion products

IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU
(Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; PROC (Process);
USES (Uses)
(FKBP, **fusion** products; DNA-binding **protein**
chimeric gene constructs, expression in eukaryote cell
and animal, and **zinc finger**- and
homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU
(Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; PROC (Process);
USES (Uses)
(FRAP, **fusion** products; DNA-binding **protein**
chimeric gene constructs, expression in eukaryote cell
and animal, and **zinc finger**- and
homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU
(Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; PROC (Process);
USES (Uses)
(FRB, **fusion** products; DNA-binding **protein**
chimeric gene constructs, expression in eukaryote cell
and animal, and **zinc finger**- and
homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU
(Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; PROC (Process);
USES (Uses)
(Krab, **fusion** products; DNA-binding **protein**
chimeric gene constructs, expression in eukaryote cell
and animal, and **zinc finger**- and
homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU
(Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; PROC (Process);
USES (Uses)
(ZFHD1, **fusion** products; DNA-binding **protein**
chimeric gene constructs, expression in eukaryote cell
and animal, and **zinc finger**- and
homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU
(Biological use, unclassified); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; PROC (Process);
USES (Uses)
(**fusion** products; DNA-binding **protein**
chimeric gene constructs, expression in eukaryote cell
and animal, and **zinc finger**- and

homeodomain-contg. **fusion** products

IT Plasmid and Episome
(p19B2F; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19B2FHH; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19B4F; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19B4FHH; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19B7F; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19B7FHH; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19BF123; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19BF1; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19BHH2F; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19BHH4F; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19BHH7F; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19BHH; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Plasmid and Episome
(p19BHHZF123; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg.

fusion products)
IT Plasmid and Episome
(p19BHHZF1; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Plasmid and Episome
(p19BCF123HH; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Plasmid and Episome
(p19BCF1HH; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(p65, **fusion** products; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing. **fusion** products)
IT Plasmid and Episome
(pCGNNF1; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Plasmid and Episome
(pCGNNF2; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Plasmid and Episome
(pCGNNF3; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Plasmid and Episome
(pCGNNF3VP16; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Plasmid and Episome
(pCGNNF3p65; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Plasmid and Episome
(pCGNNZFHD1-FKBPX3; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing. **fusion** products)
IT Plasmid and Episome
(pCGNNZFHD1-p65; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)
IT Plasmid and Episome
(pCGNNZFHD1; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-containing **fusion** products)

IT **Proteins**, biological studies
PL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prodn.; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products

IT Deoxyribonucleic acids
Ribonucleic acids
PL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(recognition; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT **Proteins**, specific or class
PL: BPN (Biosynthetic preparation); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(DNA-binding, **fusion** products; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
PL: BPN (Biosynthetic preparation); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(NF-III (nuclear factor III), **fusion** products; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
PL: BPN (Biosynthetic preparation); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(Vmw65 (virion-assocd. stimulatory **protein**, 65,000-mol.-wt.), **fusion** products; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Gene
PL: BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**chimeric**, DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Gene
PL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(expression, regulation; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
PL: BPN (Biosynthetic preparation); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(gene Egr-1, **fusion** products; DNA-binding

protein chimeric gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products

IT Therapeutics
(gene-, DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products

IT Virus, animal
(herpes simplex, VP16 **transcription** activation domain; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process)
USES (Uses)
(homeodomain-contg., **fusion** products; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Molecular association
(mol. recognition, DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT Conformation and Conformers
(**zinc-finger** motif, DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT 81458-03-9, Restriction endonuclease FokI
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cleavage domain; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

IT 9003-98-9D, DNase
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process)
USES (Uses)
(**fusion** products; DNA-binding **protein chimeric** gene constructs, expression in eukaryote cell and animal, and **zinc finger**- and homeodomain-contg. **fusion** products)

L68 ANSWER 9 OF 47 HCAPLUS COPYRIGHT 1997 ACS DUPLICATE 2
AN 1996:446671 HCAPLUS
DN 125:107092
TI p53 proteins with altered tetramerization domains, resistance to cmcp-p53 inhibition and restricted DNA binding and their therapeutic uses
IN Halazonetis, Thanos D.
PA Wistar Institute of Anatomy and Biology, USA
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
PI WO 9616989 A1 960606
DS W: AU, CA, JP, US, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 95-US15353 951127
PRAI US 94-347792 941128
US 95-431357 950428
US 95-456623 950601

DT Patent
LA English
IC ICM C07K014-82
ICS C07K019-00; C07H021-02; A61K031-70; A61K038-16
CC 3-4 Biochemical Genetics
Section cross-reference s : 1
AB p53 proteins with altered tetramerization domains that retain wild-type p53 function are described for therapeutic use. These analogs retain the ability to form tetramers and that do not hetero-oligomerize with wild-type p53 or tumor-derived p53 mutants, and may also have restricted DNA binding specificity as a result of the way that the tetramerization domain orients the DNA binding domains of the p53 tetramer relative to one another. The use of oligomerization domains from other proteins means that the transcriptional activity of the protein is not inhibited by oligomerization with the mutant form of p53 found in tumors. Genes for these proteins are also described and they may be used to manuf. the proteins or in **gene therapy**. Therapeutic uses of the proteins include strengthening the cellular response to DNA damaging agents, treating diseases characterized by abnormal cell proliferation, and inducing immune tolerance to facilitate transplants and treatment of autoimmune disease. A series of analogs in which the oligomerization domain of GCN4 or the leucine zipper of c-jun was substituted for the oligomerization domain of p53 were prepd. and shown to bind DNA. Deletion and amino acid substitution analogs of p53 were also characterized.
ST p53 analog tetramerization domain; inhibition resistant p53 analog; cjun p53 fusion protein; GCN4 p53 fusion protein
IT Neoplasm inhibitors
(p53 analogs resistant to inhibition by oncoprotein p53 as; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT Plasmid and Episome
(pGEMhump53A341, gene for p53 substitution analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT Plasmid and Episome
(pGEMhump53A344, gene for p53 substitution analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT Plasmid and Episome
(pGEMhump53D290-297, gene for p53 deletion analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT Plasmid and Episome
(pGEMhump53D290-297D300-321, gene for p53 deletion analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT Plasmid and Episome
(pGEMhump53D300-309, gene for p53 deletion analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT Plasmid and Episome
(pGEMhump53D300-317, gene for p53 deletion analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT Plasmid and Episome
(pGEMhump53D300-321, gene for p53 deletion analog on; p53

proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses

IT Plasmid and Episome
(pGEMhump53D320-327, gene for p53 deletion analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses

IT Plasmid and Episome
(pGEMhump53D364-393, gene for p53 deletion analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53H175, gene for p53 substitution analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53L337, gene for p53 substitution analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53L343RMKQ, gene for p53/GCN4 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53L346E, gene for p53/GCN4 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53L346E352I, gene for p53/GCN4 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53L347, gene for p53/GCN4 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53L355Q, gene for p53/GCN4 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53Q334, gene for p53 substitution analog on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53T323RGN, gene for p53/GCN4 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53T334GNPE, gene for p53/GCN4 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(pGEMhump53T2334NR, gene for p53/GCN4 fusion protein on; p53

proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses

IT Plasmid and Episome
(pGEMhump53TZ334NR/1352, gene for p53/GCN4 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses

IT Plasmid and Episome
(pGEMhump53junN197TZ334N, gene for c-jun/p53 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(psV2hump53junTZ334N, gene for c-jun/p53 fusion protein on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Plasmid and Episome
(psV2hump53wt, gene for p53 on; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Ribonucleic acid formation factors
PL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C/EBP (CCAAT box/enhancer element-binding protein), fusion products with p53; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Phosphoproteins
PL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Max, fusion products with p53; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Ribonucleic acid formation factors
PL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Vmw65 (virion-assocd. stimulatory protein, 65,000-mol.-wt.), fusion products with p53; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Gene
PL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**chimeric**, for p53 fusion **proteins** with **transcription factors**; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Ribonucleic acid formation factors
PL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene GCN4, fusion products with p53; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

IT Ribonucleic acid formation factors
PL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene c-jun, fusion products with p53; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and

restricted DNA binding and their therapeutic uses
IT Phosphoproteins
RL: BAC (Biological activity or effector, except adverse ; BPN (Biosynthetic preparation ; PRP (Properties ; THU (Therapeutic use ; BIOL (Biological study ; PREP (Preparation ; USES (Uses
(gene c-myc, fusion products with p53; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses
IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties ; THU (Therapeutic use ; BIOL (Biological study ; PREP (Preparation ; USES (Uses
(lactose repressors, fusion products with p53; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT Phosphoproteins
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tumor suppressor, p53, p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT 178926-74-4P 178926-75-5P 178926-76-6P 178926-77-7P
178926-78-8P 178926-79-9P 178926-80-2P 178926-81-3P
178926-82-4P 178926-83-5P 178926-84-6P 178926-85-7P
178926-86-8P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT 121939-61-5D, Phosphoprotein p 53 (human clone RP7/RP3 protein moiety reduced), mutants, analogs 178926-72-2D, 290-393-Phosphoprotein p 53 (human), mutants, analogs 178926-73-3D, 301-393-Phosphoprotein p 53 (human), mutants, analogs 178966-09-1D, 335-393-Phosphoprotein p 53 (human), mutants, analogs 178966-11-5D, 326-393-Phosphoprotein p 53 (human), mutants, analogs 178966-12-6D, 324-393-Phosphoprotein p 53 (human), mutants, analogs
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT 161247-25-2D, fusion products with p53 178926-87-9D, fusion products with p53 178966-75-8D, analogs
RL: PRP (Properties)
(amino acid sequence; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)
IT 56-86-0, Glutamic acid, miscellaneous 70-47-3, Asparagine, miscellaneous 73-32-5, Isoleucine, miscellaneous 1999-33-3, Glycylasparagine 2478-21-5 178951-06-9 178951-07-0 178951-08-1 178951-09-2
RL: MSC (Miscellaneous)
(as linker in p53 fusion proteins; p53 proteins with altered tetramerization domains, resistance to onco-p53 inhibition and restricted DNA binding and their therapeutic uses)

L68 ANSWER 6 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:724189 HCAPLUS
DN 126:2496
TI DNA-binding proteins containing **zinc finger** domains, fusion product design, and recombinant production
IN Cheng, Cheng; Young, Elton T.
STIC LIBRARY-KATHLEEN FULLER-308-4290

PA University of Washington, USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
PI WO 9632475 A2 961017
DS W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, NL, PT, SE
AI WO 96-US4793 960410
PRAI US 95-422107 950412
DT Patent
LA English
IC ICM C12N015-11
ICS C12N015-81; C07K014-395; C12N001-19
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 10
AB Methods for prepg. DNA-binding proteins having altered binding specificity are disclosed. The binding specificity of a parent DNA-binding protein comprising first and second Cys2-His2 **zinc fingers** is altered by the addn. of an addnl. **zinc finger**, wherein the altered specificity is a result of interactions between nucleotides in a target sequence and amino acid residues in each of the first, second and addnl. **zinc fingers**. The altered DNA-binding proteins are useful within methods for prepg. polypeptides.
ST **transcription factor zinc finger** fusion protein; DNA binding protein design **zinc finger**; Saccharomyces DNA binding protein **zinc finger**
IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(ADR1 (alc. dehydrogenase II gene regulatory, 1), Adr1p/F1F1F1; DNA-binding proteins contg. **zinc finger** domains, fusion product design, and recombinant prodn.)
IT Saccharomyces cerevisiae
(ADR1 or MIG1 proteins; DNA-binding proteins contg. **zinc finger** domains, fusion product design, and recombinant prodn.)
IT Molecular association
Zinc finger
(DNA-binding proteins contg. **zinc finger** domains, fusion product design, and recombinant prodn.)
IT DNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(DNA-binding proteins contg. **zinc finger** domains, fusion product design, and recombinant prodn.)
IT **Chimeric** genes
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(DNA-binding **proteins** contg. **zinc finger** domains, **fusion** product design, and recombinant prodn.)
IT Aspergillus
Escherichia coli
Eukaryote (Eukaryotae)
Fungi
Yeast
(expression host; DNA-binding proteins contg. **zinc finger** domains, fusion product design, and recombinant prodn.)
IT Ribonucleic acid formation factors

PL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(gene MIG1, fusion products; DNA-binding proteins contg. **zinc finger** domains, fusion product design, and recombinant prodn.)

IT RNA formation factors
PL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**zinc finger**-contg., fusion products; DNA-binding proteins contg. **zinc finger** domains, fusion product design, and recombinant prodn.)

IT 52-90-4DP, Cysteine, -histidine **zinc finger**
71-00-1DP, Histidine, -cysteine **zinc finger**
PL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(DNA-binding proteins contg. **zinc finger** domains, fusion product design, and recombinant prodn.)

L68 ANSWER 7 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:748823 HCAPLUS
DN 126:19536
TI Glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline
IN Efrat, Shimon
PA Albert Einstein College of Medicine of Yeshiva University, USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
PI WO 9631242 A1 961010
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 96-US4792 960403
PRAI US 95-418416 950407
DT Patent
LA English
IC ICM A61K049-00
ICS C12N015-00
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1
AB Glucose-regulated insulin producing pancreatic .beta.-cells whose proliferation is controlled by tetracyclines are described for use in the treatment of diabetes. Proliferation is controlled by a fusion protein of the tetracycline repressor tetR and VP16 to regulate expression of an SV40 T antigen gene under control of a tet operator. The gene for the fusion protein is under control an insulin-responsive promoter. An animal carrying both constructs is prepd. by crossing animals transformed with one of the constructs and .beta.-cells carrying the both constructs are selected in vitro. The construction of these cells in mice is demonstrated.
ST pancreatic beta cell proliferation control tetracycline
IT Animal cell line
(CFL-11949; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ICE (insulin control element), in promoter of gene for tetR-VP16 fusion protein; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)
IT Genes (microbial)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
chimeric, for tetR fusion **protein** with VP16, expression in animal cells of; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline

IT VP16 **transcription factor**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
fusion products with tetR, regulation of T antigen gene expression by; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline

IT Large T antigen
RL: BAC (Biological activity or effector, except adverse); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(gene for, expression in .beta.-cells of; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT Ribonucleic acid formation factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene tetR, fusion products with VP16, regulation of T antigen gene expression by; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT Antidiabetic agents
(glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT Chimeric genes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microbial, for tetR fusion protein with VP16, expression in animal cells of; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT **Genetic engineering**
(of proliferation of .beta.-cells; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT Cell proliferation
(regulation in pancreatic .beta.-cells of; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tet gene, expression of large T antigen gene from; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT Cattle
Mouse
Swine
(transgenic, pancreatic .beta.-cells of; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT Diabetes mellitus
(treatment of; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT Islet of Langerhans
(.beta.-cell; glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline)

IT 9004-10-8, Insulin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(glucose-responsive, insulin-producing transgenic pancreatic

.beta.-cells with proliferation regulated by tetracycline
IT 57-62-5, 7-Chloro-tetracycline 60-54-8, Tetracycline, derivs.
79-57-2, Oxytetracycline 564-25-0, Doxycycline 914-00-4
1665-56-1, Anhydrotetracycline 14297-95-2 61849-22-2
RL: BAC (Biological activity or effector, except adverse ; THU
(Therapeutic use); BIOL (Biological study ; USES (Uses)
glucose-responsive, insulin-producing transgenic pancreatic
.beta.-cells with proliferation regulated by tetracycline
IT 50-99-7, Glucose, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR
(Biological process); BIOL (Biological study); PROC (Process)
(.beta.-cell stimulation by; glucose-responsive,
insulin-producing transgenic pancreatic .beta.-cells with
proliferation regulated by tetracycline)

L68 ANSWER 9 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:753805 HCAPLUS
DN 126:19931
TI Differential **protein** expression vectors containing **chimeric** gene enabling production of **protein** of interest as fusion protein or alone
IN Goding, Colin Ronald; White, Michael; Yavuzer, Bahriye Ugur; Hurd, Douglas
PA Amersham International Plc, UK
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
PI WO 9630507 A2 961003
DS W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 96-GB765 960329
PRAI EP 95-302196 950331
DT Patent
LA English
IC ICM C12N015-10
ICS C12N015-62; C12N015-81; C12N015-85; C12N015-70; C12N001-19; C12Q001-68
ICI C12N001-19, C12R001-865
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 10, 16
AB This invention includes DNA constructs and vectors for differential expression of proteins in expression systems, to enable expression of a protein of interest alone or as part of a fusion protein without the need to transfer the coding sequence for the protein of interest from one vector to another. By control of transcription under different promoters, differential expression of the chimeric gene can be achieved. The **two domains** of the fusion protein are encoded by a continuous reading frame which is not interrupted by the second promoter. ATG initiation codons for the fusion and for the **second domain** are in the same reading frame. Preferably the second promoter is capable of initiating transcription of a portion of the chimeric gene encoding the **second domain** of the fusion protein without the first domain. Bacteriophage T7 promoter is a good second promoter because it is capable of initiating transcription in vitro. Plasmid pWITCH enabled prodn. of proteins tagged with an activation domain and an epitope. Plasmid pWITCH includes the galactose-inducible GAL10 promoter, herpes simplex virus VP16 activation domain, T7 bacteriophage promoter, SV5 virus epitope, polylinker DNA, and CYC transcriptional terminator sequence. Transformation of Saccharomyces cerevisiae with plasmid pWITCH resulted in efficient transcription activation with galactose and expression of PH04.DELTA.N156.
ST cloning gene differential protein expression vector; plasmid differential protein expression cloning gene; Saccharomyces cloning

differential expression vector; Escherichia cloning differential expression vector

IT Genes, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ADH1, yeast promoter; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator

IT Terminator (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(CYC; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Genes (microbial)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GAL10, galactose-inducible promoter; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Gene, microbial
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(PHO4; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Gene, microbial
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(PHO90; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(bacteriophage, yeast, or mammal; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT DNA sequences
(differential protein expression plasmid pWITCH; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Plasmids
(differential protein expression plasmid; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Genetic vectors
(differential protein expression vector; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Molecular cloning
(differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT **Fusion proteins (chimeric proteins)**
Proteins (general), preparation
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(differential **protein** expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Chimeric genes
FL: BPR Biological process ; BUU Biological use, unclassified ;
BIOL Biological study ; PROC Process ; USES Uses
differential protein expression vectors comprising
first promoter, epitope tag region, second promoter, polylinker
DNA for insertion of gene, and CYC terminator

IT SV5 virus
epitope; differential protein expression vectors comprising
first promoter, epitope tag region, second promoter, polylinker
DNA for insertion of gene, and CYC terminator

IT Escherichia coli
Saccharomyces cerevisiae
(expression host; differential protein expression vectors
comprising first promoter, epitope tag region, second promoter,
polylinker DNA for insertion of gene, and CYC terminator)

IT Antigens
FL: ANT (Analyte); BMF (Bioindustrial manufacture); BPN
(Biosynthetic preparation); ANST (Analytical study); BIOL
(Biological study); PREP (Preparation)
(fusion products, epitope-tagged; differential protein expression
vectors comprising first promoter, epitope tag region, second
promoter, polylinker DNA for insertion of gene, and CYC
terminator)

IT VP16 transcription factor
FL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation);
BIOL (Biological study); PREP (Preparation)
(fusion products, herpes simplex virus; differential protein
expression vectors comprising first promoter, epitope tag region,
second promoter, polylinker DNA for insertion of gene, and CYC
terminator)

IT GAL4 transcription factor
FL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation);
BIOL (Biological study); PREP (Preparation)
(fusion products; differential protein expression vectors
comprising first promoter, epitope tag region, second promoter,
polylinker DNA for insertion of gene, and CYC terminator)

IT Ribonucleic acid formation factors
FL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation);
BIOL (Biological study); PREP (Preparation)
(gene PHO4; differential protein expression vectors comprising
first promoter, epitope tag region, second promoter, polylinker
DNA for insertion of gene, and CYC terminator)

IT Ribonucleic acid formation factors
FL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation);
BIOL (Biological study); PREP (Preparation)
(gene PHO80; differential protein expression vectors comprising
first promoter, epitope tag region, second promoter, polylinker
DNA for insertion of gene, and CYC terminator)

IT RNA formation factors
FL: ANT (Analyte); BMF (Bioindustrial manufacture); BPN
(Biosynthetic preparation); ANST (Analytical study); BIOL
(Biological study); PREP (Preparation)
(gene lexA, DNA-binding site, fusion products; differential
protein expression vectors comprising first promoter, epitope tag
region, second promoter, polylinker DNA for insertion of gene,
and CYC terminator)

IT Deoxyribonucleic acids
FL: BUU (Biological use, unclassified); BIOL (Biological study);
USES (Uses)
(linker, polylinker; differential protein expression vectors
comprising first promoter, epitope tag region, second promoter,
polylinker DNA for insertion of gene, and CYC terminator)

IT Plasmids
(pDM22, for two-hybrid assay; differential protein expression
vectors comprising first promoter, epitope tag region, second

promoter, polylinker DNA for insertion of gene, and CYC terminator

IT Plasmids
(pEM26, for two-hybrid assay; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Plasmids
(pWITCH; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Coliphage T7
(promoter; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT Antibodies
RL: ARG (Analytical reagent use); BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(recombinant prodn. or epitope-tagged fusion product interaction; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT 71-00-1DP, Histidine, tag, fusion products with proteins
RL: ANT (Analyte); BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT 59-23-4, D-Galactose, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(galactose-inducible promoter; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

IT 172642-81-8
RL: BPR (Biological process); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleotide sequence; differential protein expression vectors comprising first promoter, epitope tag region, second promoter, polylinker DNA for insertion of gene, and CYC terminator)

L68 ANSWER 9 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:321393 HCAPLUS
DN 124:334557
TI **Transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their fusion products, and their use for target gene over-expression in cell or organism
IN Gilman, Michael Z.; Natesan, Sridaran; Pollock, Roy M.; Botfield, Martyn C.
PA USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
PI WO 9606110 A1 960229
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-US10557 950819

PRAI US 94-[illegible] 941[illegible]
US 95-[illegible] 951[illegible]
US 95-[illegible] 951[illegible]
DT Patent
LA English
IC ICM C[illegible]K014-00
ICS C12N015-00; C12N015-00; C12P021-06
CC 3-2 Biochemical Genetics
Section cross-reference(s): 12, 13
AB This invention provides novel **chimeric proteins** and DNA sequences encoding them which are useful for regulated **transcription** of target genes in genetically engineered cells or organisms cont. them. Target gene constructs and other materials useful for practicing the invention are also disclosed. Target gene constructs include a recombinant DNA sequence which is capable of binding to at least two heterologous DNA binding domains, e.g. in the form of a composite DNA binding protein or protein complex.
ST **transcription factor** chimeric gene animal cell; DNA binding **protein chimeric** gene organism; therapy gene chimeric **transcription factor** animal
IT Ribonucleic acid formation **factors**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(**fusion** products; **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)
IT Gene, animal
RL: BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(over-expression; **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)
IT Animal cell
Animal
Genetic engineering
(**transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)
IT Genetic element
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(**transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)
IT **Proteins**, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(DNA-binding, **fusion** products; **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)
IT **Proteins**, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); **PREP (Preparation)**

; USES (Uses)
(FKBP (FK 506-binding **protein**), **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)

IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); **PREP (Preparation)** ; USES (Uses)
(Vmw65 (virion-assocd. stimulatory **protein**, 65,000-mol.-wt.), **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)

IT Gene, animal
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(**chimeric**, **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)

IT Therapeutics
(geno-, **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)

IT **Proteins**, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); **PREP (Preparation)** ; USES (Uses)
(homeodomain-contg., **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)

IT Molecular association
(self-, dimerization; **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)

IT Conformation and Conformers
(**zinc-finger** motif, **transcription factors** or other DNA-binding **proteins**, **chimeric** genes encoding their **fusion** products, and their use for target gene over-expression in cell or organism)

L68 ANSWER 10 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:332747 HCAPLUS
DN 125:1377
TI **Transcription factor** CIITA fusion products with DNA-binding proteins, chimeric gene expression, and immunosuppression for treating autoimmune diseases
IN Glimcher, Laurie H.; Zhou, Hong; Douhan, John, III
PA President and Fellows of Harvard College, USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
PI WO 9606107 A1 960229
DS W: AU, CA, CN, FI, JP, KR, MX, NO, NZ, PL, RU, UA
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 95-US10691 950822
PRAI US 94-295502 940824
DT Patent
LA English
IC ICM C07H021-04

ICS C12N15-62; C12N15-12; C12P21-02; C12Q 1-68; G 1N33-50;
CC 1-7 (Pharmacology
Section cross-reference s : 3, 13, 15
AB Disclosed are methods of identifying compds. which inhibit transcription activation by CIITA and thus inhibit MHC class II gene expression. Such compds. can affect the induction of an immune response. The methods employ, independently, the activation and interactions domains of CIITA. The methods also employ the activation and interaction domains of isotype-specific CIITA proteins, allowing for the identification of compds. which are isotype-specific inhibitors of transcription and which are useful for selectively affecting the immune system.
ST human gene CIITA **transcription factor** sequence; autoimmune disease treatment CIITA fusion protein; immune suppressant CIITA fusion protein expression
IT Eukaryote
Prokaryote
(expression host cell; **transcription factor** CIITA **fusion** products with DNA-binding **proteins** , **chimeric** gene expression, and immunosuppression for treating autoimmune diseases)
IT Autoimmune disease
Immunosuppressants
Mutation
Plasmid and Episome
Protein sequences
(**transcription factor** CIITA **fusion** products with DNA-binding **proteins**, **chimeric** gene expression, and immunosuppression for treating autoimmune diseases)
IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(.alpha.-transducing factor, **fusion** products with CIITA **factor**; **transcription factor** CIITA **fusion** products with DNA-binding **proteins**, **chimeric** gene expression, and immunosuppression for treating autoimmune diseases)
IT Lymphocyte
(B-cell, **transcription factor** CIITA **fusion** products with DNA-binding **proteins**, **chimeric** gene expression, and immunosuppression for treating autoimmune diseases)
IT **Proteins**, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(DNA-binding, **fusion** products with CIITA **factor** ; **transcription factor** CIITA **fusion** products with DNA-binding **proteins**, **chimeric** gene expression, and immunosuppression for treating autoimmune diseases)
IT Gene, animal
RL: BPR (Biological process); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(HLA-DQ, **transcription factor** CIITA **fusion** products with DNA-binding **proteins**, **chimeric** gene expression, and immunosuppression for treating autoimmune diseases)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-DQ, **transcription factor** CIITA **fusion** products with DNA-binding **proteins**,

chimeric gene expression, and immunosuppression for
treating autoimmune diseases
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility antigen complex), class II,
transcription factor CIITA **fusion**
products with DNA-binding **proteins**, **chimeric**
gene expression, and immunosuppression for treating autoimmune
diseases
IT Gene, animal
RL: BPR (Biological process); BUU (Biological use, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study);
PROC (Process); USES (Uses)
(Mhc, **transcription factor** CIITA
fusion products with DNA-binding **proteins**,
chimeric gene expression, and immunosuppression for
treating autoimmune diseases)
IT Deoxyribonucleic acid sequences
(complementary, **transcription factor** CIITA
fusion products with DNA-binding **proteins**,
chimeric gene expression, and immunosuppression for
treating autoimmune diseases)
IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BUU (Biological use,
unclassified); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; USES (Uses)
(gene GAL4, **fusion** products with CIITA **factor**
; **transcription factor** CIITA **fusion**
products with DNA-binding **proteins**, **chimeric**
gene expression, and immunosuppression for treating autoimmune
diseases)
IT Ribonucleic acid formation factors
RL: BPN (Biosynthetic preparation); BUU (Biological use,
unclassified); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; USES (Uses)
(gene lexA, **fusion** products with CIITA **factor**
; **transcription factor** CIITA **fusion**
products with DNA-binding **proteins**, **chimeric**
gene expression, and immunosuppression for treating autoimmune
diseases)
IT Therapeutics
(gene-, **transcription factor** CIITA
fusion products with DNA-binding **proteins**,
chimeric gene expression, and immunosuppression for
treating autoimmune diseases)
IT 152938-72-2P
RL: BPN (Biosynthetic preparation); BUU (Biological use,
unclassified); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); **PREP (Preparation)**; USES (Uses)
(amino acid sequence; **transcription factor**
CIITA **fusion** products with DNA-binding **proteins**
, **chimeric** gene expression, and immunosuppression for
treating autoimmune diseases)
IT 177257-00-0
RL: BPR (Biological process); BUU (Biological use, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study);
PROC (Process); USES (Uses)
(nucleotide sequence; **transcription factor**
CIITA **fusion** products with DNA-binding **proteins**
, **chimeric** gene expression, and immunosuppression for
treating autoimmune diseases)

L68 ANSWER 11 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1997:51843 HCAPLUS
DN 126:100260

TI Fusion proteins of the tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes
IN Bujard, Hermann; Gossen, Manfred; Hillen, Wolfgang; Helbl, Vera; Schnappinger, Dirk
PA BASF A.-G., Germany; Knoll Aktiengesellschaft
SO U.S., 62 pp. Cont.-in-part of U.S. Ser. No. 383,754.
CODEN: USXXAM
PI US 5589362 A 961231
AI US 95-489971 950607
PRAI US 93-76726 930614
US 93-76727 930614
US 94-261452 940614
US 94-270637 940701
US 94-275976 940715
US 95-383754 950203
DT Patent
LA English
IC ICM C12P021-00
ICS C12N015-31; C07H021-04
NCL 435069100
CC 3-2 (Biochemical Genetics)
AB Fusion proteins of amino acid-substituted tet repressors and **transcription factors** that bind class B tet operators that can be used in tetracycline regulation of expression of foreign genes in eukaryotes. Genes encoding these proteins are also described. The tet operators also have nucleotide substitutions in one or two of the 3'-bases (+4 or +6). A pool of multiply mutant tet repressor genes was generated by bisulfite mutagenesis of the tetR gene and mutants with a reverse regulation phenotype (induction of gene expression by tetracyclines rather than repression) were identified using a galK/lacZ/tet operator reporter system. Fusion proteins of the N-terminal regions of these proteins and herpes simplex VP16 were prepd. by std. methods. Their efficacy was tested in a reporter gene system using the CMV promoter and a heptameric tet operator to regulate expression of a luciferase reporter in HF-5 cells. Doxycycline induced gene expression by 287-1660-fold and two genes under the control of tet operators could be induced coordinately. Fusion proteins of silencer domains, e.g. Krueppel or v-erbA proteins, are described for use as repressors. A combinatorial anal. of amino acid-substituted analogs of the repressor and base-substituted analogs of the operator was undertaken to find combinations showing the most effective induction or repression.
ST tet repressor fusion protein gene expression; operator tet operon gene regulation eukaryote; tetracycline regulation gene expression eukaryote
IT **Chimeric** genes
FL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for tetR fusion **proteins**, expression in eukaryotic cells of; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)
IT VP16 **transcription factor**
FL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fusion products with tetR repressors; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)
IT Ribonucleic acid formation factors
FL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene Krueppel, fusion products with tet repressors; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)
IT RNA formation factors

RL: BUU Biological use, unclassified ; BIOL Biological study ;
USES Uses
gene tetR, amino acid-substituted analogs, fusion products; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes

IT Proteins specific proteins and subclasses
RL: BUU Biological use, unclassified ; THU Therapeutic use ; BIOL Biological study ; USES Uses
gene v-erbA, fusion products with tet repressors; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes

IT Protein sequences
(of tet repressor analogs and fusion proteins; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT DNA sequences
(of tetR, Krueppel and v-erbA genes; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT Tetracyclines
(regulation of gene expression using; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT Operator (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(tet repressor-binding, in regulated expression of transgenes in eukaryotes; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT **Genetic engineering**
(tetracycline regulation of foreign genes in; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT Mouse
(transgenic, tetracycline regulation of foreign genes in; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT 174452-42-7
RL: BPR (Biological process); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT 174452-46-1   174452-49-4D, fusion proteins with tetR analogs
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT 174477-25-9D, fusion proteins with gene tetR repressor
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT 174452-47-2
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence, in **chimeric** genes; fusion **proteins** of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

IT 174453-68-0   174453-69-1   174453-70-4   174453-71-5   174453-72-6
RL: BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence, in regulated expression of foreign genes in

eukaryotes; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes

IT 174482-41-6 174482-45-1 174482-48-3
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes

IT 564-25-0, Doxycycline
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regulation of gene expression using; fusion proteins of tetracycline repressor for use in tetracycline regulation of gene expression in eukaryotes)

L68 ANSWER 12 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1997:7238 HCAPLUS
DN 126:55952
TI A novel member of the RING finger family, KRIP-1, associates with the KRAB-A transcriptional repressor domain of **zinc finger** proteins
AU Kim, Sung-Su; Chen, Yung-Ming; O'Leary, Eileen; Witzgall, Ralph; Vidal, Marc; Bonventre, Joseph V.
CS Renal Unit, Massachusetts General Hosp., Charlestown, MA, 02129, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1996), 93(26), 15299-15304
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 6, 13
AB The Krueppel-assocd. box A (KRAB-A) domain is an evolutionarily conserved transcriptional repressor domain present in approx. one-third of **zinc finger** proteins of the cys2-His2 type. Using the yeast two-hybrid system, we report the isolation of a cDNA encoding a novel murine protein, KRAB-A interacting protein 1 (KRIP-1) that phys. interacts with the KRAB-A region. KRIP-1 is a member of the RBCC subfamily of the RING finger, or Cys3HisCys4, family of zinc binding proteins whose other members are known to play important roles in differentiation, oncogenesis, and signal transduction. The KRIP-1 protein has high homol. to TIF1, a putative modulator of ligand-dependent activation function of nuclear receptors. A 3.5-kb mRNA for KRIP-1 is ubiquitously expressed among all adult mouse tissues studied. When a GAL4-KRIP-1 fusion protein is expressed in COS cells with a chloramphenicol acetyltransferase reporter construct with five GAL4 binding sites, there is dose-dependent repression of transcription. Thus, KRIP-1 interacts with the KRAB-A region of C2H2 **zinc finger** proteins and may mediate or modulate KRAB-A transcriptional repressor activity.
ST KRIP1 assocn KRABA transcriptional repressor domain
IT Animal tissue
(3.5-kb mRNA for KRIP-1 is ubiquitously expressed among all adult mouse tissues studied; member of the RING finger family, murine KRIP-1, assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)
IT mRNA
RL: BOC (Biological occurrence); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(3.5-kb mRNA for KRIP-1 is ubiquitously expressed among all adult mouse tissues studied; member of the RING finger family, murine KRIP-1, assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)
IT Genetic elements
RL: BAC (Biological activity or effector, except adverse); BPR

Biological process ; BIOL (Biological study ; PROC (Process
GAL4-binding site; when a GAL4-KRIP-1 fusion protein is expressed in COS cells with a chloramphenicol acetyltransferase reporter construct with five GAL4 binding sites, there is dose-dependent repression of transcription

IT Proteins (specific proteins and subclasses), biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(KRIP-1; novel member of the RING finger family, murine KRIP-1, assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)

IT Proteins (specific proteins and subclasses), biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RING finger zinc-binding; novel member of the RING finger family, murine KRIP-1, assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)

IT Proteins (specific proteins and subclasses), biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TIF1; murine KRIP-1 protein has high homol. to TIF1, a putative modulator of ligand-dependent activation function of nuclear receptors)

IT cDNA sequences
(for murine KRIP-1, which assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)

IT Mouse
(novel member of the RING finger family, murine KRIP-1, assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)

IT Protein sequences
(of murine KRIP-1, which assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)

IT **Transcription factors**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(repressors, KRAB-A-contg.; novel member of the RING finger family, murine KRIP-1, assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)

IT COS cell
Transcription repression
(when a GAL4-KRIP-1 fusion protein is expressed in COS cells with a chloramphenicol acetyltransferase reporter construct with five GAL4 binding sites, there is dose-dependent repression of transcription)

IT GAL4 **transcription factor**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(when a GAL4-KRIP-1 fusion protein is expressed in COS cells with a chloramphenicol acetyltransferase reporter construct with five GAL4 binding sites, there is dose-dependent repression of transcription)

IT **Fusion proteins** (**chimeric proteins**)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(when a GAL4-KRIP-1 **fusion protein** is expressed in COS cells with a chloramphenicol acetyltransferase reporter construct with five GAL4 binding sites, there is dose-dependent repression of transcription)

IT 185229-45-2
RL: PRP (Properties)
(amino acid sequence; novel member of the RING finger family, murine KRIP-1, assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins)

IT 192331-09-5, GenBank U67303

FL. PPP Properties
nucleotide sequence; novel member of the RING finger family, murine KRIP-1, assocs. with the KRAB-A transcriptional repressor domain of **zinc finger** proteins

L69 ANSWER 13 OF 47 MEDLINE
AN 96312899 MEDLINE
TI pH-dependent enhancement of DNA binding by the ultrabithorax **homeodomain**.
AU Li L; von Kessler D; Beachy P A; Matthews K S
CS Department of Biochemistry and Cell Biology, Rice University, Houston, Texas 77251, USA.
NC GM22441 (NIGMS)
SO BIOCHEMISTRY, (1996 Jul 30) 35 (30) 9832-9.
Journal code: A0G. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9611
AB Ultrabithorax (Ubx) and Deformed (Dfd) proteins of Drosophila melanogaster contain **homeodomains** (HD) that are structurally similar and recognize similar DNA sequences, despite functionally distinct genetic regulatory roles for Ubx and Dfd. We report in the present study that Ubx-HD binding to a single optimal target site displayed significantly increased affinity and higher salt concentration dependence at lower pH, while Dfd-HD binding to DNA was unaffected by pH. Results from studies of chimeric Ubx-Dfd **homeodomains** showed that the N- and C-terminal regions of the Ubx-HD are required for this pH dependence. The increase in binding affinity at lower pH was greater for the Ubx optimal binding site than for other DNA binding sites, indicating that subtle sequence alterations in DNA binding sites may influence pH-dependent behavior. These data demonstrate enhanced DNA binding affinity at lower pH for the Ubx-HD in vitro and suggest the potential for significant discrimination of DNA binding sites in vivo.
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Base Sequence
Binding Sites
Chimeric Proteins: CH, chemistry
Chimeric Proteins: ME, metabolism
Crystallography, X-Ray
Drosophila melanogaster: ME, metabolism
DNA: CH, chemistry
*DNA: ME, metabolism
DNA-Binding Proteins: CH, chemistry
*DNA-Binding Proteins: ME, metabolism
Homeodomain Proteins: CH, chemistry
***Homeodomain Proteins: ME, metabolism**
Hydrogen-Ion Concentration
Insect Hormones: ME, metabolism
Kinetics
Models, Molecular
Molecular Sequence Data
*Nucleic Acid Conformation
Oligodeoxyribonucleotides: CH, chemistry
*Oligodeoxyribonucleotides: ME, metabolism
*Protein Structure, Secondary
Structure-Activity Relationship
Transcription Factors: ME, metabolism
RN 9007-49-2 (DNA)
CN 0 (engrail protein, Drosophila); 0 (ultrabithorax protein); 0 (**Chimeric Proteins**); 0 (Dfd protein); 0

DNA-Binding Proteins ; **Homeodomain** Proteins ;
Insect Hormones ; Oligodeoxyribonucleotides ;
Transcription Factors

L69 ANSWER 14 OF 47 HCAPLUS COPYRIGHT 1997 ACS DUPLICATE 3
AN 1996:571132 HCAPLUS
DN 125:266936
TI Constitutive retinoid receptors expressed from adenovirus vectors that specifically activate chromosomal target genes required for differentiation of promyelocytic leukemia and teratocarcinoma cells
AU Lipkin, Steven M.; Grider, Teresa L.; Heyman, Richard A.; Glass, Christopher K.; Gage, Fred H.
CS Laboratory Genetics, Salk Institute Biological Studies, La Jolla, CA, 92037, USA
SO J. Virol. (1996), 70(10), 7182-7189
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 14
AB Sufficient knowledge of **transcription factor** structure and function has accumulated to allow attempts at the rational design of novel **transcription factors** for the study of gene regulation and potential application in **gene therapy**. In the present studies, we have systematically evaluated the function of chimeric retinoid receptors generated by fusion with the transactivation domain of VP16 and expression in adenovirus vectors. By varying the location of fusion of the VP16 transactivation domain with the retinoic acid receptor (RAR) or retinoid X receptor (RXR), marked differences in the specificity of gene activation were obtained. Although several **chimeric proteins** activated both RAR and RXR target genes, fusion of the VP16 transactivation domain to the N terminus of RAR permitted specific activation of reporter genes contg. retinoic acid response elements. In contrast, fusion of the VP16 transactivation domain to the C terminus of RXR permitted specific activation of reporter genes contg. RXR response elements. When tested for their ability to activate chromosomal targets, the chimera consisting of VP16 linked to the N terminus of RAR was much more active in promoting the differentiation of HL-60 cells and NTera-2 cells than the chimera consisting of VP16 linked to the C terminus of RXR. These observations support the existence of two distinct retinoid signalling pathways predicted on the basis of biochem. and pharmacol. studies and provide direct evidence that the programs of differentiation elicited by retinoic acid in these cells are mediated by a specific subset of binding sites for RAR-RXR heterodimers. VP16-RAR and VP16-RXR fusion proteins should be of further use in dissecting the relative contributions of RARs and RXRs to specific programs of gene expression. Constitutive retinoid receptors may also be considered for use as novel tumor suppressor genes for genetically based treatment of retinoid-responsive cancers.
ST retinoid receptor adenovirus vector differentiation leukemia; teratocarcinoma differentiation retinoid receptor adenovirus vector
IT Cell differentiation
(constitutive retinoid receptors expressed from adenovirus vectors specifically activate chromosomal target genes required for differentiation of promyelocytic leukemia and teratocarcinoma cells)
IT Gene, animal
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(constitutive retinoid receptors expressed from adenovirus vectors specifically activate chromosomal target genes required for differentiation of promyelocytic leukemia and teratocarcinoma

cells
IT Chromosome
genes; constitutive retinoid receptors expressed from adenovirus vectors specifically activate chromosomal target genes required for differentiation of promyelocytic leukemia and teratocarcinoma cells
IT Genetic element
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
retinoid X responsive element; fusion of the VP16 transactivation domain to the C terminus of RXR permitted specific activation of reporter genes contg. RXR response elements)
IT Animal cell line
(HL-60, chimera consisting of VP16 linked to the N terminus of RAR was much more active in promoting the differentiation of HL-60 cells and NTera-2 cells than the chimera consisting of VP16 linked to the C terminus of RXR)
IT Animal cell line
(NTera2, chimera consisting of VP16 linked to the N terminus of RAR was much more active in promoting the differentiation of HL-60 cells and NTera-2 cells than the chimera consisting of VP16 linked to the C terminus of RXR)
IT Genetic element
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(RARE (retinoic acid-responsive element), fusion of VP16 transactivation domain to the N terminus of RAR permitted specific activation of reporter genes contg. retinoic acid response elements)
IT Receptors
Retinoid receptors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(RXR (retinoid X receptor), fusion of the VP16 transactivation domain to the C terminus of RXR permitted specific activation of reporter genes contg. RXR response elements)
IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(Vmw65 (virion-assocd. stimulatory protein, 65,000-mol.-wt.), fusion of VP16 transactivation domain to the N terminus of RAR permitted specific activation of reporter genes contg. retinoic acid response elements)
IT Virus, animal
(adeno-, constitutive retinoid receptors expressed from adenovirus vectors specifically activate chromosomal target genes required for differentiation of promyelocytic leukemia and teratocarcinoma cells)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(fusion products, systematic evaluation of the function of chimeric retinoid receptors generated by fusion with the transactivation domain of VP16 and expression in adenovirus vectors)
IT Therapeutics
(gene-, constitutive retinoid receptors expressed from adenovirus vectors specifically activate chromosomal target genes required for differentiation of promyelocytic leukemia and teratocarcinoma cells)
IT Leukemia
(promyelocytic, constitutive retinoid receptors expressed from adenovirus vectors specifically activate chromosomal target genes required for differentiation of promyelocytic leukemia and

teratocarcinoma cells
IT Receptors
FL: BAC Biological activity or effector, except adverse ; BPR Biological process ; BIOL Biological study ; PROC Process
retinoic acid, fusion of VP16 transactivation domain to the N terminus of RAR permitted specific activation of reporter genes contg. retinoic acid response elements
IT Carcinoma
(tera-, constitutive retinoid receptors expressed from adenovirus vectors specifically activate chromosomal target genes required for differentiation of promyelocytic leukemia and teratocarcinoma cells)

L68 ANSWER 15 OF 47 MEDLINE
AN 96209811 MEDLINE
TI Dimerization specificity of Arabidopsis MADS domain homeotic proteins APETALA1, APETALA3, PISTILLATA, and AGAMOUS.
AU Riechmann J L; Krizek B A; Meyerowitz E M
CS Division of Biology, California Institute of Technology, Pasadena, 91125, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 May 14) 93 (10) 4793-8.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9609
AB The MADS domain homeotic proteins APETALA1 (AP1), APETALA3 (AP3), PISTILLATA (PI), and AGAMOUS (AG) act in a combinatorial manner to specify the identity of Arabidopsis floral organs. The molecular basis for this combinatorial mode of action was investigated. Immunoprecipitation experiments indicate that all four proteins are capable of interacting with each other. However, these proteins exhibit "partner-specificity" for the formation of DNA-binding dimers; only AP1 homodimers, AG homodimers, and AP3/PI heterodimers are capable of binding to CArG-box sequences. Both the AP3/PI heterodimer and the AP1 or AG homodimers are formed when the three corresponding proteins are present together. The use of **chimeric proteins** formed by domain swapping indicates that the L region (which follows the MADS box) constitutes a key molecular determinant for the selective formation of DNA-binding dimers. The implications of these results for the ABC genetic model of flower development are discussed.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.
Amino Acid Sequence
*Arabidopsis: CH, chemistry
Arabidopsis: GD, growth & development
Arabidopsis: GE, genetics
Base Sequence
Chimeric Proteins: CH, chemistry
Chimeric Proteins: GE, genetics
Chimeric Proteins: ME, metabolism
DNA Probes: GE, genetics
DNA-Binding Proteins: CH, chemistry
DNA-Binding Proteins: GE, genetics
DNA-Binding Proteins: ME, metabolism
DNA, Plant: GE, genetics
DNA, Plant: ME, metabolism
Genes, Homeobox
Genes, Plant
***Homeodomain Proteins: CH, chemistry**
Homeodomain Proteins: GE, genetics
Homeodomain Proteins: ME, metabolism
Molecular Sequence Data

*Plant Proteins: CH, chemistry
Plant Proteins: GE, genetics
Plant Proteins: ME, metabolism
Protein Binding
Protein Conformation
Sequence Homology, Amino Acid
Transcription Factors: CH, chemistry
Transcription Factors: GE, genetics
Transcription Factors: ME, metabolism
CN (apetala 1 protein); (AGAMOUS protein ; **Chimeric Proteins**); (DNA Probes); (DNA-Binding Proteins); (DNA, Plant); (**Homeodomain** Proteins); (MADS-box protein, plant); (Plant Proteins); (PISTILLATA protein); (**Transcription** Factors)

L68 ANSWER 16 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 97:15998 BIOSIS
DN 99815201
TI Neither the **homeodomain** nor the activation domain of Bicoid is specifically required for its down-regulation by the Torso receptor tyrosine kinase cascade.
AU Bellaiche Y; Bandyopadhyay P; Desplan C; Desplan N
CS Howard Hughes Med. Inst., Rockefeller Univ., New York, NY 10021, USA
SO Development (Cambridge) 122 (11). 1996. 3499-3509. ISSN: 0950-1991
LA English
PR Biological Abstracts Vol. 103 Iss. 002 Ref. 019315
AB Bicoid (Bcd) is a maternal morphogen responsible for patterning the head and thorax of the Drosophila embryo. Correct specification of head structure, however, requires the activity of the Torso receptor tyrosine kinase cascade, which also represses expression of Bcd targets at the most anterior tip of the embryo. Here, we investigate the role of both the **homeodomain** (HD) and the activation domain of Bcd in the anterior repression of its targets. When a Bcd mutant protein whose HD has been replaced by the Gal4 DNA-binding domain is expressed in early embryos, a reporter gene driven by Gal4 DNA-binding sites is first activated in an anterior domain and then repressed from the anterior pole. The down-regulation of Bcd-Gal4 activity requires torso function but does not depend on endogenous bcd activity, indicating that the Bcd protein alone and none of its targets is required to mediate the effect of torso. Functional analysis of a **chimeric protein**, whose activation domain has been replaced by a generic activation domain, indicates that the activation domain of Bcd is also not specifically required for its down-regulation by Torso. We propose that Torso does not affect the ability of Bcd to bind DNA, but instead directs modification of Bcd or of a potential Bcd co-factor, which renders the Bcd protein unable to activate **transcription**.
ST RESEARCH ARTICLE; DROSOPHILA; EMBRYO; MOLECULAR GENETICS; DEVELOPMENT; BICOID; ACTIVATION DOMAIN; **HOMEODOMAIN**; MORPHOGEN; TORSO RECEPTOR TYROSINE KINASE CASCADE; TORSO GENE; HEAD PATTERNING; THORAX PATTERNING; DOWN-REGULATION; **TRANSCRIPTION**
RN 80449-02-1 (TYROSINE KINASE)
CC Genetics and Cytogenetics-Animal *09516
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Enzymes-Physiological Studies *10909
Developmental Biology-Embryology-Morphogenesis, General *25509
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology *64076
BC Diptera 75914

L68 ANSWER 17 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1997:91672 HCAPLUS
DN 126:155909
TI EAT-2 is a novel SH2 domain containing protein that is up regulated by Ewing's sarcoma EWS/FLI1 fusion gene

AU Thompson, Andrew D.; Braun, Benjamin S.; Arvand, Afsane; Stewart, Sophia E.; May, William A.; Chen, Emily; Korenberg, Julie; Denny, Christopher

CS Molecular Biology Institute, School Medicine, University California, Los Angeles, CA, 90095, USA

SO Oncogene (1996 , 13 12 , 2649-2658
CODEN: ONCNES; ISSN: 0950-9232

DT Journal

LA English.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3

AB The EWS/FLI1 fusion protein is created by the translocation between chromosomes 11 and 22 that appears in most Ewing's sarcomas. This **chimeric protein** has been demonstrated to be an aberrant **transcription factor**. Genes up regulated by EWS/FLI1 but not by full-length FLI1 were identified by representational difference anal. (RDA). The authors have characterized a novel gene, EWS/FLI1 activated transcript 2 (EAT-2) that was cloned from a murine cDNA library using a differentially expressed RDA fragment. EAT-2 expression is seen within 4-8 h of EWS/FLI1 induction. Its expression correlates with transformation of NIH3T3 cells by **chimeric proteins** related to EWS/FLI1 but not by unrelated genes. EAT-2 is expressed in normal murine tissues and contains a unique but biochem. functional SH2 domain. An homologous sequence in the human genome has been identified and mapped to chromosome 1q22. Human EAT-2 transcripts were identified by reverse transcriptase-polymerase chain reaction (RT-PCR) in Ewing's sarcoma cell tumor cell lines. EAT-2's unique structure and correlation with transformation make it a candidate for playing a role in the transformation of NIH3T3 cells and the oncogenesis of Ewing's sarcoma.

ST Ewing sarcoma EAT2 protein EWS FLI1; sequence EAT2 protein DNA human mouse

IT Genes (animal)
Proteins (specific proteins and subclasses)
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(EAT-2; human and mouse EAT-**2** are SH2 **domain** -contg. proteins that are up-regulated by Ewing's sarcoma EWS/FLI1 fusion gene)

IT **Chimeric** genes
Fusion proteins (**chimeric proteins**)
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(EWS/FLI1; human and mouse EAT-**2** are SH2 **domain** -contg. **proteins** that are up-regulated by Ewing's sarcoma EWS/FLI1 **fusion** gene)

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(EWS; human and mouse EAT-**2** are SH2 **domain** -contg. proteins that are up-regulated by Ewing's sarcoma EWS FLI1 fusion gene)

IT Genes (animal)
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(FLI1; human and mouse EAT-**2** are SH2 **domain** -contg. proteins that are up-regulated by Ewing's sarcoma EWS/FLI1 fusion gene)

IT Proteins (specific proteins and subclasses)
RL: ADV (Adverse effect, including toxicity); BOC (Biological

occurrence ; BPR Biological process ; BIOL Biological study ; OCCU Occurrence ; PROC Process
gene EWS; human and mouse EAT-2 are SH2 **domain**-contg. proteins that are up-regulated by Ewing's sarcoma EWS/FLI1 fusion gene
IT RNA formation factors
RL: ARU (Adverse effect, including toxicity ; BIOL Biological occurrence ; BPR (Biological process ; BIOL Biological study ; OCCU (Occurrence); PROC (Process)
(gene FLI1; human and mouse EAT-2 are SH2 **domain**-contg. proteins that are up-regulated by Ewing's sarcoma EWS/FLI1 fusion gene)
IT Ewing's sarcoma
Gene expression
SH2 domain
(human and mouse EAT-2 are SH2 **domain**-contg. proteins that are up-regulated by Ewing's sarcoma EWS/FLI1 fusion gene)
IT Genetic mapping
Human chromosome 1
(mapping of human EAT-2 protein gene)
IT cDNA sequences
DNA sequences
Protein sequences
(sequences of human genomic and mouse cDNA EAT-2 protein)

L68 ANSWER 18 OF 47 MEDLINE
AN 96202477 MEDLINE
TI Functional domains in the Deformed protein.
AU Zhu A; Muzzio M A
CS Department of Biological Sciences, University of Pittsburgh, PA 15260, USA.
SO DEVELOPMENT, (1996 May) 122 (5) 1577-87.
Journal code: ECW. ISSN: 0950-1991.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9609
AB A **chimeric protein** consisting of Deformed with a substituted Abdominal-B **homeodomain** (Dfd/Abd-B) is used to identify protein domains outside the **homeodomain** that are required for regulatory activity in vivo. A series of deletion proteins were generated based on regions showing amino acid composition similar to known regulatory domains. Each mutant protein can influence regulation of homeotic genes in a manner distinct from the intact protein. Activity was also tested using promoter elements from empty spiracles and Distal-less, two genes known to be directly regulated by Abdominal-B. Removal of the acidic region and the C-tail region convert the chimera from a strong activator to a repressor of the Distal-less element, but had comparatively little effect on the activation of the empty spiracles element. Constructs without a **third domain**, the N domain, fail to show any regulatory activity. The N domain is the only domain of the Dfd/Abd-B protein which exhibits significant activation activity when fused to a heterologous DNA **binding** domain. Our results suggest transcriptional activity of the N domain can be modulated by the acidic and C-tail domains.
CT Check Tags: Animal
Amino Acid Sequence
Base Sequence
Chimeric Proteins: GE, genetics
Chimeric Proteins: ME, metabolism
Drosophila: EM, embryology
*Drosophila: GE, genetics

*Gene Expression Regulation, Developmental
Genes, Homeobox
Genes, Reporter
Homeodomain Proteins: GE, genetics
***Homeodomain Proteins: ME, metabolism**
Molecular Sequence Data
Promoter Regions, Genetic
Protein Binding
Sequence Deletion
Structure-Activity Relationship
Transcription Factors: GE, genetics
***Transcription Factors: ME, metabolism**
Transcription, Genetic
CN (empty spiracles protein); (Abd-B proteins); (**Chimeric Proteins**); (Dfd protein); (Distal-less protein-1); (**Homeodomain** Proteins); (**Transcription** Factors)

L68 ANSWER 19 OF 47 MEDLINE
AN 97115703 MEDLINE
TI Transgenic analysis of a potential Hoxd-11 limb regulatory element present in tetrapods and fish.
AU Beckers J; Gerard M; Duboule D
CS Department of Zoology and Animal Biology, University of Geneva, Sciences III, Quai Ernest Ansermet 30, Geneva 4, 1211, Switzerland.. duboule@sc2a.unige.ch
SO DEVELOPMENTAL BIOLOGY, (1996 Dec 15) 180 (2) 543-53.
Journal code: E7T. ISSN: 0012-1606.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9703
EW 19970304
AB Genes of the HoxD complex related to the Drosophila Abd-B gene are involved in the morphogenesis of vertebrate paired appendages. Hoxd-11, for instance, is necessary in combination with other Hox genes for the proper development of different parts of the tetrapod limbs. Sequence comparisons between the mouse, chicken, and zebrafish Hoxd-11 loci have revealed the conservation of several blocks of DNA sequence which may be of importance for the regulation of Hoxd-11 expression. We have used transgenic mice to show that one of these conserved elements specifically drives expression in a proximal-posterior part of developing forelimbs. Production of mice transgenic for a full fish Hoxd-11 construct as well as for mouse-fish Hoxd-11 chimeric constructs shows that the fish counterpart of this sequence is able to elicit expression in mouse forelimbs as well, though in a slightly different domain. However, this fish element requires the presence of the mouse promoter and does not work in its own context. These results are discussed in light of both the control of Hoxd gene expression during limb development and the use of a comparative interspecies approach to understand the regulation of genes involved in vertebrate development.
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
Base Sequence
Chickens
Chimeric Proteins: BI, biosynthesis
Cloning, Molecular
Drosophila
DNA Primers
*Forelimb: GD, growth & development
*Gene Expression Regulation, Developmental
Genes, Homeobox
***Homeodomain Proteins: BI, biosynthesis**
Homeodomain Proteins: GE, genetics

Limb Bud: PH, physiology
Mice
Mice, Transgenic
Molecular Sequence Data
Morphogenesis
Polymerase Chain Reaction
Promoter Regions (Genetics)
*Regulatory Sequences, Nucleic Acid
Restriction Mapping
Sequence Homology, Nucleic Acid
***Transcription Factors: BI, biosynthesis**
Transcription Factors: GE, genetics
Vertebrates
Zebrafish
CN 0 (**Chimeric Proteins**); 0 (DNA Primers); 0 (**Homeodomain** Proteins); 0 (HoxD-11 protein); 0 (**Transcription** Factors)

L68 ANSWER 20 OF 47 MEDLINE
AN 96193673 MEDLINE
TI Novel, high expressing and antibiotic-controlled plasmid vectors designed for use in **gene therapy**.
AU Liang X; Hartikka J; Sukhu L; Manthorpe M; Hobart P
CS Department of Molecular Biology, Vical Incorporated, San Diego, CA 92121, USA.
SO GENE THERAPY, (1996 Apr) 3 (4) 350-6.
Journal code: GDE. ISSN: 0969-7128.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9612
AB The promise of effective **gene therapy** can only be accomplished by high-level expression and regulatable delivery of gene products. To achieve this end, a eukaryotic expression plasmid was modified to make **transcription** dependent on a tetracycline(Tc)-regulated chimeric transactivator. Mouse muscle injected with this two plasmid cis/trans control system expressed reporter proteins at levels five- to 10-fold greater than the cytomegalovirus immediate-early promoter-controlled parental plasmid. Tetracycline could be useful to either repress or activate transactivator-controlled expression based on the position of the tetO control sequences within the reporter plasmid. Finally, a prototype single plasmid construct was made and shown to express a self-regulating bicistronic transcript containing both the reporter and the transactivator. These Tc-controlled plasmids, termed maximum expression and regulated vectors (MERVs), have the potential to target a variety of **gene therapy** applications.
CT Check Tags: Animal; Human
Antibiotics, Tetracycline: PD, pharmacology
Base Sequence
Cell Line
Chimeric Proteins: GE, genetics
Chloramphenicol O-Acetyltransferase: GE, genetics
Cytomegalovirus: GE, genetics
DNA, Recombinant: GE, genetics
Gene Expression
***Gene Therapy: MT, methods**
*Genetic Vectors
Mice
Molecular Sequence Data
Muscles: ME, metabolism
*Plasmids: GE, genetics
Tetracycline: PD, pharmacology
Trans-Activation (Genetics)

Trans-Activators: GE, genetics
RN 60-54-8 (Tetracycline)
CN EC 2.3.1.28 (Chloramphenicol Acetyltransferase ; 1 Antibiotics, Tetracycline ; 2 **Chimeric Proteins** ; 3 DNA, Recombinant ; 4 Genetic Vectors ; 5 Plasmids ; 6 Trans-Activators)

L68 ANSWER 21 OF 47 MEDLINE
AN 96191615 MEDLINE
TI Designing of chimeric DNA/RNA hammerhead ribozymes to be targeted against AML1/MTG8 mRNA.
AU Mizu T; Sueoka E; Okabe S; Sueoka N; Komori A; Fujiki H
CS Department of Immunology and Virology, Saitama Cancer Center Research Institute, Japan.
SO JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY, (1996) 122 (4) 254-6.
Journal code: HL5. ISSN: 0171-5216.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9607
AB For therapeutic purposes, two chimeric DNA/RNA hammerhead ribozymes were synthesized to cleave AML1/MTG8, the t(8;21)-associated fusion mRNA of acute myeloid leukemia. One ribozyme, A/MRZ-1, recognizes the area adjacent to the fusion point between AML1 and MTG8, and cleaves six bases downstream from this point. The other, MRZ-1, recognizes the MTG8 sequence. Both ribozymes cleaved synthetic chimeric DNA/RNA substrates at theoretical sites. Neither cleaved AML1 RNA. A/MRZ-1 cleaved only AML1/MTG8 RNA, and MRZ-1 cleaved both AML1/MTG8 and MTG8 RNAs. The two ribozymes showed growth inhibition of an acute myeloid leukemia cell line carrying t(8;21), SKNO-1 cells. The same extent of growth inhibition was attained by antisense oligonucleotides against AML1/MTG8 RNA. The results suggest that the ribozyme has the potential to be developed as a useful agent for **gene therapy**, in particular for leukemia with t(8;21).
CT Check Tags: Human
*Antineoplastic Agents: CH, chemistry
Base Sequence
Chimeric Proteins
DNA: CH, chemistry
*DNA-Binding Proteins: GE, genetics
Growth Inhibitors
Leukemia, Myeloid: GE, genetics
*Leukemia, Myeloid: TH, therapy
Molecular Sequence Data
*Neoplasm Proteins: GE, genetics
RNA, Catalytic: CH, chemistry
*RNA, Catalytic: TU, therapeutic use
RNA, Messenger: GE, genetics
RNA, Neoplasm: GE, genetics
***Transcription Factors**: GE, genetics
Translocation (Genetics)
Tumor Cells, Cultured
RN 9007-49-2 (DNA)
CN 0 (Antineoplastic Agents); 0 (AML1 protein); 0 (**Chimeric Proteins**); 0 (DNA-Binding Proteins); 0 (Growth Inhibitors); 0 (MTG8 protein); 0 (Neoplasm Proteins); 0 (RNA, Catalytic); 0 (RNA, Messenger); 0 (RNA, Neoplasm); 0 (**Transcription** Factors)

L68 ANSWER 22 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:693046 HCAPLUS
DN 126:154112
TI Characterization of a leucine-zipper-like domain in Vpr protein of

human immunodeficiency virus type 1
AU Wang, Lilin; Mukherjee, Sampa; Narayan, Opendra; Zhao, Ling-Jun
CS Marion Merrell Dow Foundation, Laboratory of Viral Pathogenesis, Department of Microbiology, Molecular Genetics, Immunology, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS, 66160-7424, USA
SO Gene (1996), 178(1/2), 7-13
CODEN: GENEDE; ISSN: 0378-1119
DT Journal
LA English
CC 6-3 (General Biochemistry)
Section cross-reference(s): 3, 10
AB Human immunodeficiency virus type 1 (HIV-1) replicates productively in vitro in CD4+-T cells and/or macrophages. In the host, however, HIV-1 replication may be restricted by the quiescence of susceptible cells. Vpr is a 15-kDa late viral gene product, which is assembled in the virion and suspected to enhance HIV-1 replication in the infected host. We demonstrated previously that Vpr interacted specifically with the cellular **transcription factor** Sp1, and activated transcription from the HIV-1 long-terminal-repeat. Both Vpr-Sp1 interaction and trans-activation by Vpr required a central Leu/Ile-rich domain (LR domain, aa 60-81) in Vpr. This domain of Vpr was also found crit. for Vpr interaction with another cellular protein of 180kDa. We now provide biochem. evidence that the Vpr LR-domain has a leucine-zipper-like structure. The leucine-zipper structure has been found in a variety of cellular **transcription factors**, which use the leucine-zipper domain to form a specific dimer before they can bind to DNA through an upstream basic domain. The LR domain of HIV-1 Vpr, when fused to the basic domain of the cellular **transcription factor** CREB, was capable of supporting specific DNA binding by the CREB basic domain. Point mutational anal. of the Leu/Ile residues in the LR domain suggested that multiple Leu/Ile residues may be involved in maintaining the leucine-zipper-like structure. Mutagenesis in the context of the full-length Vpr also helped identify Leu/Ile residues crit. for Vpr interaction with the cellular 180-kDa protein. These results suggested that the leucine-zipper-like domain may be an important functional determinant for HIV-1 Vpr.
ST HIV1 Vpr protein LR domain; Sp1 HIV1 Vpr interaction LR domain
IT Protein motifs
(LR domain (Leu/Ile-rich domain); characterization of a leucine-zipper-like domain (Leu/Ile-rich LR domain) in Vpr protein of human immunodeficiency virus type 1, domain required for interaction with Sp1 and a 180kD cellular protein)
IT Human immunodeficiency virus 1
Leucine zipper
(characterization of a leucine-zipper-like domain (Leu/Ile-rich LR domain) in Vpr protein of human immunodeficiency virus type 1)
IT Transcription activation
(characterization of a leucine-zipper-like domain (Leu/Ile-rich LR domain) in Vpr protein of human immunodeficiency virus type 1, domain required for interaction with Sp1 and a 180kD cellular protein)
IT Sp1 **transcription factor**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
characterization of a leucine-zipper-like domain (Leu/Ile-rich LR domain) in Vpr protein of human immunodeficiency virus type 1, domain required for interaction with Sp1 and a 180kDa cellular protein)
IT **Fusion proteins (chimeric proteins)**
RL: EAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BIOL (Biological study); **PREP**

(Preparation)
construction of a **transcription factor**
CREB-Vpr LR domain **fusion protein** and use to
det. the function of the LR domain

IT Proteins (specific proteins and subclasses)
RL: BAC (Biological activity or effector, except adverse ; BPR
(Biological process) ; PRP (Properties) ; BIOL (Biological study) ;
PROC (Process)
(gene vpr; characterization of a leucine-zipper-like domain
(Leu/Ile-rich LR domain) in Vpr protein of human immunodeficiency
virus type 1, domain required for interaction with Sp1 and a
180kD cellular protein)

IT Protein sequences
(of the LR domain of the Vpr protein in human immunodeficiency
virus type 1)

IT 196799-39-5
RL: BAC (Biological activity or effector, except adverse); BPR
(Biological process); PRP (Properties); BIOL (Biological study);
PROC (Process)
(amino acid sequence; of the LR domain of the Vpr protein in
human immunodeficiency virus type 1)

L68 ANSWER 23 OF 47 MEDLINE
AN 96064753 MEDLINE
TI Redundant domains contribute to the transcriptional activity of the thyroid **transcription** factor 1.
AU De Felice M; Damante G; Zannini M; Francis-Lang H; Di Lauro R
CS Stazione Zoologica Anton Dohrn, Villa Comunale, Napoli, Italy.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Nov 3) 270 (44) 26649-56.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9602
AB The thyroid **transcription** factor 1 (TTF-1) is a **homeodomain**-containing protein implicated in the activation of thyroid-specific gene expression. Here we report that TTF-1 is capable of activating **transcription** from thyroglobulin and, to a lesser extent, thyroperoxidase gene promoters in nonthyroid cells. Full transcriptional activation of the thyroglobulin promoter by TTF-1 requires the presence of at least two TTF-1 binding sites. TTF-1 activates **transcription** via two functionally redundant transcriptional activation domains that as suggested by competition experiments, could use a common intermediary factor.
CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
Base Sequence
Binding Sites
Cell Line
Chimeric Proteins: BI, biosynthesis
Chimeric Proteins: ME, metabolism
Gene Expression Regulation
Hela Cells
Homeodomain Proteins: CH, chemistry
***Homeodomain Proteins: ME, metabolism**
Molecular Sequence Data
Mutagenesis, Insertional
Nuclear Proteins: BI, biosynthesis
*Nuclear Proteins: CH, chemistry
*Nuclear Proteins: ME, metabolism
Oligodeoxyribonucleotides
*Promoter Regions (Genetics)
Rats

Recombinant Proteins: CH, chemistry
Recombinant Proteins: ME, metabolism
*Thyroglobulin: BI, biosynthesis
Thyroglobulin: GE, genetics
*Thyroid Gland: ME, metabolism
Trans-Activation (Genetics
Transcription Factors: BI, biosynthesis
***Transcription Factors: CH, chemistry**
***Transcription Factors: ME, metabolism**
***Transcription, Genetic**
Transfection
TATA Box
RN 9010-34-3 (Thyroglobulin)
CN 0 (thyroid nuclear factor 1); 0 **Chimeric Proteins**
); 0 (**Homeodomain** Proteins); 0 (Nuclear Proteins); 0
(Oligodeoxyribonucleotides); 0 (Recombinant Proteins); 0 (
Transcription Factors)

L68 ANSWER 24 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:550903 BIOSIS
DN 98565203
TI Protein Kinase A-dependent Transactivation by the E2A-Pbx1 Fusion Protein.
AU Ogo A; Waterman M R; Kamps M P; Kagawa N
CS Dep. Biochem., Vanderbilt Univ. Sch. Med., Nashville, TN 37232-0146, USA
SO Journal of Biological Chemistry 270 (43). 1995. 25340-25343. ISSN: 0021-9258
LA English
PR Biological Abstracts Vol. 101 Iss. 001 Ref. 008008
AB The chimeric gene E2A-PBX1 is formed by the t(1;19) chromosomal translocation exclusively associated with pediatric pre-B cell acute lymphoblastic leukemia (pre-B ALL). The resultant fusion **protein** from this **chimeric** gene contains the DNA-binding **homeodomain** of Pbx1. The first and only functional Pbx1 binding site has been localized in bovine CYP17 to a sequence (CRS1) that participates in cAMP-dependent **transcription** of this gene encoding the steroid hydroxylase, 17-alpha-hydroxylase cytochrome P450. Because Pbx1 is not expressed in pre-B cells, it may be possible that the E2a-Pbx1 fusion protein expressed in pre-B cells having this translocation will activate, in response to cAMP, **transcription** of genes not normally expressed in these cells leading to arrest of differentiation at the pre-B cell stage. We have now shown that reporter genes comprising CRS1 are activated transcriptionally by protein kinase A (PKA) in the pre-B cell line 697, which endogenously expresses the fusion protein, and that overexpression of E2A-Pbx1 in additional cell lines enhances **transcription** of reporter genes in a PKA-dependent fashion. Thus, it seems plausible that arrest in the pre-B stage leading to pre-B ALL includes cAMP-dependent activation of E2A-Pbx1.
ST RESEARCH ARTICLE; HUMAN; CHIMERIC GENE; DNA-BINDING **HOMEODOMAIN**; PEDIATRIC PRE-B CELL ACUTE LYMPHOBLASTIC LEUKEMIA; CHROMOSOMAL TRANSLOCATION; CYCLIC AMP DEPENDENT ACTIVATION; REPORTER GENES
RN 60-92-4 (CYCLIC AMP)
142009-29-5 (PROTEIN KINASE A)
CC Cytology and Cytochemistry-Human *02508
Genetics and Cytogenetics-Human *03508
Biochemical Methods-Proteins, Peptides and Amino Acids *10054
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics-General Biophysical Techniques *10504
Biophysics-Membrane Phenomena *10509
Blood, Blood-Forming Organs and Body Fluids-Blood, Lymphatic and

Reticuloendothelial Pathologies *15016
Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System *15018
Neoplasms and Neoplastic Agents-Biochemistry *24016
Neoplasms and Neoplastic Agents-Blood and Reticuloendothelial Neoplasms *24019
BC Hominidae 66215

L68 ANSWER 25 OF 47 MEDLINE
AN 96003857 MEDLINE
TI Analysis of **homeodomain** function by structure-based design of a **transcription** factor.
AU Pomerantz J L; Pabo C O; Sharp P A
CS Center for Cancer Research, Harvard-Massachusetts Institute of Technology, Cambridge, MA 02139, USA..
NC P01-CA42063 (NCI)
P30-CA14051 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Oct 10) 92 (21) 9752-6.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9601
AB The **homeodomain** is a 60-amino acid module which mediates critical protein-DNA and protein-protein interactions for a large family of regulatory proteins. We have used structure-based design to analyze the ability of the Oct-1 **homeodomain** to nucleate an enhancer complex. The Oct-1 protein regulates herpes simplex virus (HSV) gene expression by participating in the formation of a multiprotein complex (C1 complex) which regulates alpha (immediate early) genes. We recently described the design of ZFHD1, a chimeric **transcription** factor containing zinc fingers 1 and 2 of Zif268, a four-residue linker, and the Oct-1 **homeodomain**. In the presence of alpha-transinduction factor and C1 factor, ZFHD1 efficiently nucleates formation of the C1 complex in vitro and specifically activates gene expression in vivo. The sequence specificity of ZFHD1 recruits C1 complex formation to an enhancer element which is not efficiently recognized by Oct-1. ZFHD1 function depends on the recognition of the Oct-1 **homeodomain** surface. These results prove that the Oct-1 **homeodomain** mediates all the protein-protein interactions that are required to efficiently recruit alpha-transinduction factor and C1 factor into a C1 complex. The structure-based design of **transcription** factors should provide valuable tools for dissecting the interactions of DNA-bound domains in other regulatory circuits.
CT Check Tags: Comparative Study; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Base Sequence
Binding, Competitive
Chimeric Proteins: ME, metabolism
*DNA-Binding Proteins
DNA-Binding Proteins: GE, genetics
*DNA-Binding Proteins: ME, metabolism
*Gene Expression Regulation
Homeodomain Proteins: GE, genetics
***Homeodomain Proteins: ME, metabolism**
Models, Molecular
Molecular Sequence Data
Protein Binding
Recombinant Fusion Proteins: GE, genetics
Recombinant Fusion Proteins: ME, metabolism

Structure-Activity Relationship
*Transcription Factors
Transcription Factors: GE, genetics
*Transcription Factors: ME, metabolism
Transfection
CN (Chimeric Proteins); (DNA-Binding Proteins);
(Homeodomain Proteins); (Oct-1 protein); (
Recombinant Fusion Proteins; (Transcription Factors;
(ZFHD1 protein)

L68 ANSWER 26 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:512439 BIOSIS
DN 95517439
TI Expression of the unc-4 homeoprotein in Caenorhabditis elegans motor neurons specifies presynaptic input.
AU Miller D M III; Niemeyer C J
CS Dep. Cell Biol., Vanderbilt Univ. Med. Cent., Nashville, TN 37232, USA
SO Development (Cambridge) 121 (9). 1995. 2877-2886. ISSN: 0950-1991
LA English
PR Biological Abstracts Vol. 100 Iss. 011 Ref. 168345
AB In the nematode, Caenorhabditis elegans, VA and VB motor neurons arise from a common precursor cell but adopt different morphologies and synapse with separate sets of interneurons in the ventral nerve cord. A mutation that inactivates the unc-4 **homeodomain** gene causes VA motor neurons to assume the VB pattern of synaptic input while retaining normal axonal polarity and output; the disconnection of VA motor neurons from their usual presynaptic partners blocks backward locomotion. We show that expression of a functional unc-4-beta-galactosidase **chimeric protein** in VA motor neurons restores wild-type movement to an unc-4 mutant. We propose that unc-4 controls a differentiated characteristic of the VA motor neurons that distinguishes them from their VB sisters, thus dictating recognition by the appropriate interneurons. Our results show that synaptic choice can be controlled at the level of **transcription** in the post-synaptic neuron and identify a homeoprotein that defines a subset of cell-specific traits required for this choice.
ST RESEARCH ARTICLE; CAENORHABDITIS ELEGANS; UNC-4-BETA-GALACTOSIDASE; INTERNEURON
CC Cytology and Cytochemistry-Animal *02506
Biochemical Studies-Proteins, Peptides and Amino Acids 10064
Enzymes-Physiological Studies *10808
Metabolism-Proteins, Peptides and Amino Acids *13012
Nervous System-Physiology and Biochemistry *20504
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Aschelminthes *64016
BC Nematoda 51300

L68 ANSWER 27 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS DUPLICATE 4
AN 95:220476 BIOSIS
DN 95234776
TI High mobility group protein 2 functionally interacts with the POU domains of octamer **transcription** factors.
AU Cwilling S; Koenig H; Wirth T
CS Centrum Mol. Biol. Heidelberg, Im Neuenheimer Feld 282, D-69120 Heidelberg, Germany
SO EMBO (European Molecular Biology Organization) Journal 14 (6). 1995. 1198-1208. ISSN: 0261-4189
LA English
PR Biological Abstracts Vol. 099 Iss. 011 Ref. 154952
AB The octamer **transcription** factors Oct1 and Oct2 are involved in the transcriptional regulation of both lymphoid-specific and ubiquitously expressed genes. Their activity depends critically on their interaction with distinct cellular cofactors. Therefore, we

have isolated cDNAs encoding proteins that physically interact with Oct2. Here we describe the analysis of one such clone, representing the murine homologue of high mobility group HMG protein 2. We have mapped the interaction domains for both proteins and have shown that HMG2 and Oct2 interact via their HMG domains and POU **homeodomains**, respectively. This interaction is not restricted to Oct2, as other members of the octamer **transcription** factor family like Oct1 and Oct6 also interact with HMG2. The interaction with HMG2 results in a marked increase in the sequence-specific DNA binding activity of the Oct proteins. Interestingly, the HMG2 protein is not present in the protein-DNA complex detected by an electrophoretic mobility shift assay. The Oct and HMG2 proteins also interact in vivo. A **chimeric protein**, in which the strong transactivation domain of VP16 was fused directly to the HMG domains of HMG2, stimulated the activity of an octamer-dependent reporter construct upon cotransfection. Furthermore, the expression of antisense RNA for HMG2 specifically reduces octamer-dependent **transcription**. These results suggest that one of the functions of HMG2 is to support the octamer **transcription** factors in their role as transcriptional activators.

ST RESEARCH ARTICLE; MURINE HOMOLOGUE; DNA REPLICATION; TRANSCRIPTIONAL ACTIVATOR

CC Cytology and Cytochemistry-Animal *02506
Genetics and Cytogenetics-Animal *03506
Biochemical Methods-Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Methods-Proteins, Peptides and Amino Acids 10054
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10900
Biophysics-General Biophysical Techniques 10504
In Vitro Studies, Cellular and Subcellular 32600

BC Muridae 86375

L68 ANSWER 29 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS

AN 95:266582 BIOSIS

DN 98290982

TI Functional interactions between YY1 and adenovirus E1A.

AU Lee J-S; See R H; Galvin K M; Wang J; Shi Y

CS Dep. Pathol., Harvard Med. Sch., 200 Longwood Ave., Boston, MA 02115, USA

SO Nucleic Acids Research 23 (6). 1995. 925-931. ISSN: 0305-1048

LA English

PR Biological Abstracts Vol. 100 Iss. 001 Ref. 005720

AB YY1 is a C-2H-2-type **zinc** finger **transcription** factor that is a member of the human GLI-Kruppel family of proteins. YY1 represses **transcription** when bound upstream of **transcription** initiation sites. The repression can be relieved by adenovirus E1A and activation of target genes occurs. We have mapped the repression domain of YY1 to the C-terminal region, overlapping its DNA **binding** domain. We have also identified an activation domain within the first 69 amino acids of YY1. The YY1 C-terminal region is involved in physical interactions with E1A and is functionally necessary for YY1 to respond to E1A. This suggests that relief of YY1 repression by E1A involves YY1-E1A physical interactions. Although not involved in interactions with E1A, the N-terminal activation domain is also necessary for YY1 to respond to E1A. Presumably, under repressing conditions, the activation domain is masked by the conformation of YY1, but is released upon **binding** of E1A and is required to subsequently activate **transcription**. Consistent with this hypothesis, an ATF-2-YY1 **chimeric protein** containing the activation **domain** of ATF-2 and the C-terminal two-thirds of YY1 is still a potent repressor. Unlike the mutant YY1 lacking its own N-terminal activation domain, the **chimeric**

protein is fully responsive to E1A.
ST RESEARCH ARTICLE; GENE EXPRESSION REGULATION; **TRANSCRIPTION** FACTOR; STRUCTURE-ACTIVITY RELATIONSHIP; DNA-**BINDING** PROTEIN; PROTEIN-PROTEIN INTERACTION
CC Genetics and Cytogenetics-General *13502
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10160
Biochemical Studies-Proteins, Peptides and Amino Acids *10164
Replication, Transcription, Translation *10300
Virology-Animal Host Viruses *38506
BC Adenoviridae 02611

L68 ANSWER 29 OF 47 MEDLINE
AN 95375235 MEDLINE
TI The homeobox gene ATK1 of Arabidopsis thaliana is expressed in the shoot apex of the seedling and in flowers and inflorescence stems of mature plants.
AU Dockx J; Quaedvlieg N; Keultjes G; Kock P; Weisbeek P; Smeekens S
CS Department of Molecular Cell Biology, University of Utrecht, The Netherlands..
SO PLANT MOLECULAR BIOLOGY, (1995 Jul) 28 (4) 723-37.
Journal code: A60. ISSN: 0167-4412.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X81353; GENBANK-X81354
EM 9512
AB The **homeodomain** is a DNA-binding domain present in a large family of eukaryotic regulatory proteins. **Homeodomain** proteins have been shown to play key roles in controlling developmental programs in various organisms. Here we report the isolation and characterisation of a homeobox gene from Arabidopsis thaliana designated ATK1. The gene was isolated using as a probe the homeobox domain of the KN1 gene from maize. The **homeodomain** of ATK1 is highly homologous to the **homeodomain** of the KN1 gene of maize (81%) but shows only poor homology outside the **homeodomain**. Therefore ATK1 is probably not the Arabidopsis homologue of the KN1 gene from maize. It contains the four invariant amino acid residues present in the recognition helix 3 of all other **homeodomain** proteins. Outside the **homeodomain** a region rich in aspartate and glutamate residues is found suggesting that ATK1 is a transcriptional activator. The gene contains four introns which is similar in the KN1 gene of maize and the Oshl gene of rice. Primer extension reveals the presence of two **transcription** initiation sites. The leader sequence of the genuine transcript is 342 nucleotides long and contains two upstream open reading frames. ATK1 is strongly expressed in the shoot apex of seedlings, while in mature plants the gene is primarily expressed in flowers and inflorescence stems. Such an expression pattern is reminiscent of that of the KN1 gene of maize and therefore ATK1 could similarly be involved in determining cell fate.
CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Amino Acid Sequence
*Arabidopsis: GE, genetics
Base Sequence
Binding Sites
Chimeric Proteins
DNA, Complementary: GE, genetics
Gene Expression Regulation, Developmental
*Gene Expression Regulation, Plant
*Genes, Homeobox: GE, genetics
*Genes, Plant: GE, genetics
Genomic Library
Histocytochemistry
***Homeodomain Proteins**: GE, genetics**

Molecular Sequence Data
Plant Shoots: GE, growth & development
Plants, Transgenic
Selection (Genetics)
Sequence Analysis, DNA
Sequence Homology, Amino Acid
Species Specificity
Tissue Distribution
***Trans-Activators: GE, genetics**
Transcription, Genetic
Transformation, Genetic
CN 0 (ATK1 protein); 0 (**Chimeric Proteins**); 0 (DNA, Complementary); 0 (**Homeodomain** Proteins); 0 (Trans-Activators)
GEN ATK1

L68 ANSWER 30 OF 47 MEDLINE
AN 95247029 MEDLINE
TI Pbx proteins display hexapeptide-dependent cooperative DNA binding with a subset of Hox proteins.
AU Chang C P; Shen W F; Rozenfeld S; Lawrence H J; Largman C; Cleary M L
CS Department of Pathology, Stanford University Medical Center, California 94305, USA.
NC CA42971 (NCI)
SO GENES AND DEVELOPMENT, (1995 Mar 15) 9 (6) 663-74.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9508
AB The human proto-oncogene PBX1 codes for a homolog of Drosophila extradenticle, a divergent homeo domain protein that modulates the developmental and DNA-binding specificity of select HOM proteins. We demonstrate that wild-type Pbx **proteins** and **chimeric** E2a-Pbx1 oncoproteins cooperatively bind a consensus DNA probe with HoxB4, B6, and B7 of the Antennapedia class of Hox/HOM proteins. Specificity of Hox-Pbx interactions was suggested by the inability of Pbx proteins to cooperatively bind the synthetic DNA target with HoxA10 or Drosophila even-skipped. Site-directed mutagenesis showed that the hexapeptide motif (IYPWMK) upstream of the Hox homeo domain was essential for HoxB6 and B7 to cooperatively bind DNA with Pbx proteins. Engraftment of the HoxB7 hexapeptide onto HoxA10 endowed it with robust cooperative properties, demonstrating a functional role for the highly conserved hexapeptide element as one of the molecular determinants delimiting Hox-Pbx cooperativity. The Pbx homeo domain was necessary but not sufficient for cooperativity, which required conserved amino acids carboxy-terminal of the homeo domain. These findings demonstrate that interactions between Hox and Pbx proteins modulate their DNA-binding properties, suggesting that Pbx and Hox proteins act in parallel as heterotypic complexes to regulate expression of specific subordinate genes.
CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Base Sequence
Chimeric Proteins: ME, metabolism
Conserved Sequence
Drosophila: GE, genetics
*DNA: ME, metabolism
DNA-Binding Proteins: GE, genetics
*DNA-Binding Proteins: ME, metabolism
Evolution

Homeodomain Proteins: GE, genetics
***Homeodomain Proteins: ME, metabolism**
Molecular Sequence Data
Nucleic Acid Hybridization
Oncogene Proteins, Fusion: GE, genetics
Oncogene Proteins, Fusion: ME, metabolism
Precipitin Tests
Protein Binding
*Proto-Oncogene Proteins: ME, metabolism
Structure-Activity Relationship
Transcription Factors: GE, genetics
Transcription Factors: ME, metabolism

RN 146151-85-9 (oncoprotein E2A-Pbx1); 164394-16-1 (Hoxa-10 protein); 9007-49-2 (DNA)

CN 0 (proto-oncogene protein pbx1); 0 (**Chimeric Proteins**); 0 (DNA-Binding Proteins); 0 (**Homeodomain** Proteins); 0 (Hoxb-4 protein); 0 (HoxB6 protein); 0 (HoxB7 protein); 0 (Oncogene Proteins, Fusion); 0 (Proto-Oncogene Proteins); 0 (**Transcription** Factors)

L68 ANSWER 31 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1995:970495 HCAPLUS
DN 124:25782
TI Derepression of the activity of genetically engineered heat shock factor causes constitutive synthesis of heat shock proteins and increased thermotolerance in transgenic Arabidopsis
AU Lee, Jeong Hee; Huebel, Anja; Schoeffl, Fritz
CS Universitaet Tuebingen, Tuebingen, D-72076, Germany
SO Plant J. (1995), Volume Date 1995, 8(4), 603-12
CODEN: PLJUED; ISSN: 0960-7412
DT Journal
LA English
CC 11-4 (Plant Biochemistry)
AB ATHSF1 is a heat shock **transcription factor** (HSF) of Arabidopsis that is constitutively expressed but its activity for DNA binding, trimer formation and transcriptional activation of heat shock (hs) genes is repressed at normal temps. In this study the functional properties of **chimeric** HSF-glucuronidase (GUS) fusion **proteins** were tested. Ectopic expression of HSF-GUS or GUS-HSF in transgenic Arabidopsis plants resulted in a derepression of HSF functions as shown by trimer formation, specific DNA binding, and the constitutive expression of heat shock proteins (HSPs) at normal temp. A novel GUS activity-staining protocol was used to show the specific binding of trimeric HSF fusion proteins to DNA and following hs, an interaction between chimeric HSF-GUS and authentic HSF proteins. The chimeric HSFs were insensitive to the neg. regulation that counteracts activation of the authentic HSF at normal temp. Heterotrimer complexes were reconstituted in vitro from recombinant ATHSF1 and HSF-GUS proteins expressed in Escherichia coli and using this protocol, the temp.-dependent activation of wt HSF was monitored in vivo and in vitro. Transgenic plants expressing constitutively active HSF-GUS fusion proteins are also constitutive for HSPs. Approx. 20% of the max. heat-inducible levels of HSP18 were already present at normal temp. The level of basic thermotolerance was significantly enhanced in these plants. The results indicate that **genetic engineering** using protein fusion is a very effective means to derepress the activity of an important regulatory protein in plants, that consequently activates a constitutive hs response in the absence of heat stress and eventually alters the thermotolerance phenotype.
ST Arabidopsis HSF transgenic thermotolerance
IT Ribonucleic acid formation factors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(ATHSF1; derepression of the activity of genetically engineered heat shock factor causes constitutive synthesis of heat shock proteins and increased thermotolerance in transgenic Arabidopsis

IT **Genetic engineering**
Transformation, genetic
(derepression of the activity of genetically engineered heat shock factor causes constitutive synthesis of heat shock proteins and increased thermotolerance in transgenic Arabidopsis

IT Arabidopsis thaliana
(transgenic; derepression of the activity of genetically engineered heat shock factor causes constitutive synthesis of heat shock proteins and increased thermotolerance in transgenic Arabidopsis)

IT Plant stress
(heat, derepression of the activity of genetically engineered heat shock factor causes constitutive synthesis of heat shock proteins and increased thermotolerance in transgenic Arabidopsis)

IT Proteins, specific or class
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(heat-shock, derepression of the activity of genetically engineered heat shock factor causes constitutive synthesis of heat shock proteins and increased thermotolerance in transgenic Arabidopsis)

L68 ANSWER 32 OF 47 MEDLINE
AN 96195802 MEDLINE
TI Analysis of the heavy metal-responsive **transcription** factor MTF-1 from human and mouse.
AU Muller H P; Brungnera E; Georgiev O; Badzong M; Muller K H; Schaffner W
CS Institut fur Molekularbiologie (II) der Universitat Zurich, Switzerland.
SO SOMATIC CELL AND MOLECULAR GENETICS, (1995 Sep) 21 (5) 289-97. Journal code: UY2. ISSN: 0740-7750.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9608
AB Heavy metal-induced **transcription** in mammalian cells is conferred by the metal-responsive 70 kDa **transcription** factor MTF-1 which contains six **zinc** fingers and at least **three** activation **domains**. In previous cell transfection experiments we have shown that the **zinc** finger region confers an about 3 fold metal inducibility of **transcription**, due to its differential **zinc** **binding**. However, we also noted that human MTF-1 was more metal-responsive than the mouse factor (about 10 fold versus 3 fold, respectively). Here we analyze this difference in more detail by using chimeric human-mouse factors and narrow the critical region to a 64 amino acid stretch immediately downstream of the **zinc** fingers, overlapping with the acidic activation domain. A short human segment of this region (aa 313-377) confers efficient metal induction to the mouse MTF-1 when replacing the corresponding mouse region. However, high metal inducibility requires an unaltered MTF-1 and is lost when human MTF-1 is fused to the general activation domain of herpesvirus VP16. Wild type and truncation mutants of MTF-1 fused to VP16 yield chimeras of high transcriptional activity, some exceeding the wildtype regulator, but only limited (about 3 fold) heavy metal inducibility.
CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence

Chimeric Proteins: BI, biosynthesis
Chimeric Proteins: ME, metabolism
Gene Expression: DE, drug effects
Hela Cells
Herpes Simplex Virus Protein Vmw65: BI, biosynthesis
Herpes Simplex Virus Protein Vmw65: ME, metabolism
Mammals
Metals: PD, pharmacology
Mice
Molecular Sequence Data
Restriction Mapping
Sequence Homology, Amino Acid
Sequence Homology, Nucleic Acid
Trans-Activation (Genetics)
Transcription Factors: BI, biosynthesis
Transcription Factors: GE, genetics
***Transcription Factors: ME, metabolism**
Transcription, Genetic: DE, drug effects
Zinc Fingers
3T3 Cells

CN 0 (**transcription** factor MTF-1); 0 (**Chimeric Proteins**); 0 (Herpes Simplex Virus Protein Vmw65); 0 (Metals); 0 (**Transcription** Factors)

L68 ANSWER 33 OF 47 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:737232 HCAPLUS
DN 126:85533
TI Interference of Myb transactivation activity by a conditional dominant negative protein: functional interference in a cytotoxic T-cell line results in G1 arrest
AU Lyon, Jonathan J.; Watson, Roger J.
CS Ludwig Institute for Cancer Research, Imperial College School of Medicine at St. Mary's, Norfolk Place, London, W2 1PG, UK
SO Gene (1995), Volume Date 1996, 182(1/2), 123-128
CODEN: GENED6; ISSN: 0378-1119
DT Journal
LA English
CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 13, 15
AB The ability to ablate the activity of specific **transcription factors** in vivo is a potentially important tool to study their roles in cellular processes such as the cell cycle. Previously, prodn. of a dominant interfering c-Myb protein (comprising a fusion of the c-Myb DNA binding domain with the Drosophila Engrailed transrepressor) was found to inhibit the proliferation of immature thymocytes in the developing thymus of transgenic mice. We report here the further development of this stratagem by rendering the c-Myb/Engrailed protein conditionally active by fusion to a modified estrogen receptor hormone binding domain, ER. Co-transfection expts. in NIH 3T3 fibroblasts showed that the resulting chimeric protein, Myb/En/ER, repressed transactivation of a c-Myb-responsive reporter only in the presence of the synthetic steroid, 4-hydroxytamoxifen (OHT). Addnl., we found that Myb/En/ER could counteract transactivation by C/EBP-.beta. of the mim-1 promoter, which contains juxtaposed Myb and C/EBP binding sites. Cytotoxic T-cells stably producing the inactive Myb/En/ER protein were readily obtained by gene transfection. The addn. of OHT to these cells resulted in inhibition of proliferation and arrest in G1. The utility of this exptl. system to study Myb and other **transcription factors** is discussed.
ST G1 arrest dominant interfering Myb protein; T cell proliferation interference Myb protein; mim1 promoter CEBPbeta interference Myb protein
IT Genetic element

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(MRE (gene c-myb RNA formation factor-responsive element); Myb/En/ER chimeric protein interference with transactivation of mim-1 promoter by **transcription factor** C/EBP-.beta.)

IT **Fusion proteins** (**chimeric proteins**)
RL: BAC (Biological activity or effector, except adverse); BSP (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); **PREP (Preparation)**; PROC (Process)
(Myb/En/ER (c-Myb DNA-binding domain/Engrailed transrepressor/estrogen receptor hormone-binding domain); functional interference with Myb transactivation activity in cytotoxic T-cell line results in G1 arrest)

IT **Transcription factor** NF-IL6
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Myb/En/ER chimeric protein interference with transactivation of mim-1 promoter by **transcription factor** C/EBP-.beta.)

IT G1 phase
(arrest; functional interference with Myb transactivation activity in cytotoxic T-cell line results in G1 arrest)

IT Transcription repression
(functional interference with Myb transactivation activity by Myb/En/ER chimeric protein in cytotoxic T-cell line results in G1 arrest)

IT Cell cycle
Cytotoxic T cell
T-cell proliferation
(functional interference with Myb transactivation activity in cytotoxic T-cell line results in G1 arrest)

IT c-Myb protein
PL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(functional interference with Myb transactivation activity in cytotoxic T-cell line results in G1 arrest)

IT **Proteins**, specific or class
PL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(gene engrailed, Myb/En/ER **fusion** product; functional interference with Myb transactivation activity by Myb/En/ER **chimeric protein** in cytotoxic T-cell line results in G1 arrest)

IT Promoter (genetic element)
PL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(mim-1; Myb/En/ER chimeric protein interference with transactivation of mim-1 promoter by **transcription factor** C/EBP-.beta.)

IT Estrogen receptors
PL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(modified hormone binding domain of, Myb/En/ER **fusion** product contg.; functional interference with Myb transactivation activity by Myb/En/ER **chimeric protein** in cytotoxic T-cell line results in G1 arrest)

IT 68047-06-3, 4-Hydroxytamoxifen
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Myb/En/ER **fusion protein** activation by; functional interference with Myb transactivation activity by

Myb-En EP **chimeric protein** in cytotoxic
T-cell line results in G1 arrest

L69 ANSWER 34 OF 47 MEDLINE
AN 95059069 MEDLINE
TI Transformation properties of the E2a-Pbx1 chimeric oncoprotein: fusion with E2a is essential, but the Pbx1 **homeodomain** is dispensable.
AU Monica K; LeBrun D P; Dedera D A; Brown R; Cleary M L
CS Department of Pathology, Stanford University Medical Center, California 94305.
NC CA42971 (NCI)
SO MOLECULAR AND CELLULAR BIOLOGY, (1994 Dec) 14 (12) 8304-14.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9502
AB The t(1;19) chromosomal translocation in acute lymphoblastic leukemias creates chimeric E2a-Pbx1 oncoproteins that can act as DNA-binding activators of **transcription**. A structural analysis of the functional domains of E2a-Pbx1 showed that portions of both E2a and Pbx1 were essential for transformation of NIH 3T3 cells and transcriptional activation of synthetic reporter genes containing PBX1 consensus binding sites. Hyperexpression of wild-type or experimentally truncated Pbx1 proteins was insufficient for transformation, consistent with their inability to activate **transcription**. When fused with E2a, the Pbx-related proteins Pbx2 and Pbx3 were also transformation competent, demonstrating that all known members of this highly similar subfamily of **homeodomain** proteins have latent oncogenic potential. The oncogenic contributions of E2a to the chimeras were localized to transactivation motifs AD1 and AD2, as their mutation significantly impaired transformation. Either the **homeodomain** or Pbx1 amino acids flanking this region could mediate transformation when fused to E2a. However, the **homeodomain** was not essential for transformation, since a mutant E2a-Pbx1 protein (E2a-Pbx delta HD) lacking the **homeodomain** efficiently transformed fibroblasts and induced malignant lymphomas in transgenic mice. Thus, transformation mediated by the chimeric oncoprotein E2a-Pbx1 is absolutely dependent on motifs acquired from E2a but the Pbx1 **homeodomain** is optional. The latter finding suggests that E2a-Pbx1 may interact with cellular proteins that assist or mediate alterations in gene expression responsible for oncogenesis even in the absence of **homeodomain**-DNA interactions.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Adenovirus E2 Proteins: PH, physiology
*Cell Transformation, Neoplastic
Chimeric Proteins
*DNA-Binding Proteins: CH, chemistry
DNA-Binding Proteins: PH, physiology
*Gene Expression Regulation, Developmental
*Genes, Homeobox
***Homeodomain Proteins: CH, chemistry**
Homeodomain Proteins: ME, metabolism
***Homeodomain Proteins: PH, physiology**
Lymphoma: GE, genetics
Lymphoma: PA, pathology
Mice
Mice, Transgenic
*Oncogene Proteins, Fusion: PH, physiology
*Proto-Oncogene Proteins: CH, chemistry
Proto-Oncogene Proteins: ME, metabolism

Structure-Activity Relationship
***Transcription Factors: PH, physiology**
3T3 Cells
RN 146180-81-4 (proto-oncogene protein Pbx3 ; 146181-85-9 (oncoprotein E2A-Pbx1)
CN 0 (proto-oncogene protein pbx1); 0 (proto-oncogene protein Pbx2 ; 0 (Adenovirus E2 Proteins); 0 (**Chimeric Proteins** ; 0 (DNA-Binding Proteins); 0 (**Homeodomain** Proteins ; 0 (Oncogene Proteins, Fusion); 0 (Proto-Oncogene Proteins); 0 (**Transcription** Factors)

L68 ANSWER 35 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 94:485154 BIOSIS
DN 97419154
TI A differential response element for the homeotics at the Antennapedia P1 promoter of Drosophila.
AU Saffman E E; Krasnow M A
CS Dep. Biochem., Stanford Univ., Stanford, CA 94305, USA
SO Proceedings of the National Academy of Sciences of the United States of America 91 (16). 1994. 7420-7424. ISSN: 0027-8424
LA English
PR Biological Abstracts Vol. 098 Iss. 007 Ref. 089966
AB Homeotic genes encode DNA-binding **transcription** factors that specify the identity of a segment or segments in particular body regions of Drosophila. The developmental specificity of these proteins results from their differential regulation of various target genes. This specificity could be achieved by use of different regulatory elements by the homeoproteins or by use of the same elements in different ways. The Ultrabithorax (UBX), abdominal-A (ABD-A), and Antennapedia (ANTP) homeoproteins differentially regulate the Antennapedia P1 promoter in a cell culture cotransfection assay: UBX and ABD-A repress, whereas ANTP activates P1. Either of two regions of P1 can confer this pattern of differential regulation. One of the regions lies downstream and contains homeoprotein-binding sites flanking a 37-bp region called BetBS. ANTP protein activates **transcription** through the binding sites, whereas UBX and ABD-A both activate **transcription** through BetBS and use the flanking binding sites to prevent this effect. Thus, homeoproteins can use the same regulatory element but in very different ways. **Chimeric** UBX-ANTP **proteins** and UBX deletion derivatives demonstrate that functional specificity in P1 regulation is dictated mainly by sequences outside the **homeodomain**, with important determinants in the N-terminal region of the proteins.
ST RESEARCH ARTICLE; DNA; **TRANSCRIPTION** FACTOR; PROTEIN; ULTRABITHORAX; ABDOMINAL-A
CC Genetics and Cytogenetics-Animal *03506
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies-Proteins, Peptides and Amino Acids 10064
Replication, Transcription, Translation *10300
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology *64076
Invertebrate Body Regions and Structures-Thorax 64208
Invertebrate Body Regions and Structures-Abdomen 64210
Invertebrate Body Regions and Structures-Appendages 64212
BC Diptera 75314

L68 ANSWER 36 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS DUPLICATE 5
AN 95:109021 BIOSIS
DN 98122321
TI Direct analysis of native and **chimeric** GATA specific DNA **binding proteins** from Aspergillus nidulans.
AU Peters D G; Caddick M X
CS Dep. Genetics Microbiol., Donnan Lab., Univ. Liverpool, PO Box 147, Liverpool L69 3BX, UK

SO Nucleic Acids Research 22 24 , 1994. 5164-5172. ISSN: 0305-1048
LA English
PR Biological Abstracts Vol. 099 Iss. 006 Ref. 078878
AB In Aspergillus nidulans the regulatory gene areA is responsible for mediating nitrogen metabolite repression. The areA product (AREA) represents an example of the GATA family of DNA **binding** proteins, which are characterized by the presence of a GATA domain consisting of a **zinc** finger within a highly conserved region of 52 amino acids. Among the other **transcription** factors included in this family is the principal erythroid **transcription** factor, GATA-1, which contains **two** GATA **domains**. In order to demonstrate high specificity **binding** of native AREA to DNA containing the sequence -GATA-, and investigate the presence in A. nidulans of other proteins with related specificities, we have used gel mobility shift assays. Both AREA-dependent and independent complexes have been identified. Two strains bearing chimeric genes were also characterized. In these, the region encoding the native GATA domain of AREA was replaced by sequences from murine GATA-1 cDNA encoding either the equivalent C-terminal domain or both the N and C-terminal domains. Strains bearing the areA::NC-GATA construct, which includes the sequence encoding both the N and C-terminal domains of GATA-1, leads to a pronounced increase in one of two AREA-dependent complexes and implicates the N-terminal domain of GATA-1 in mediating protein-protein interactions.
ST RESEARCH ARTICLE; ASPERGILLUS NIDULANS; AREA GENE; REGULATORY GENE; NITROGEN METABOLITE REPRESSION; PROTEIN-PROTEIN INTERACTION
RN 7727-37-9 (NITROGEN)
CC Cytology and Cytochemistry-Plant *01504
Genetics and Cytogenetics-Plant *03504
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics-Molecular Properties and Macromolecules *10506
Metabolism-Nucleic Acids, Purines and Pyrimidines *13014
Plant Physiology, Biochemistry and Biophysics-Chemical Constituents *51522
BC Fungi Imperfecti or Deuteromycetes 15500

L68 ANSWER 37 OF 47 MEDLINE
AN 94309626 MEDLINE
TI Functional differences between HOX proteins conferred by two residues in the **homeodomain** N-terminal arm.
AU Phelan M L; Sadoul R; Featherstone M S
CS McGill Cancer Centre, McGill University, Montreal, Quebec, Canada..
SO MOLECULAR AND CELLULAR BIOLOGY, (1994 Aug) 14 (8) 5066-75.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9410
AB Hox genes encode **homeodomain**-containing transcriptional regulators that function during development to specify positional identity along embryonic axes. The **homeodomain** is composed of a flexible N-terminal arm and three alpha helices, and it differentially binds DNA. A number of **homeodomains** recognize sites containing a TAAT core motif. The product of the murine Hoxd-4 (Hox-4.2) gene functions in a positive autoregulatory fashion in P19 cells that is dependent on two TAAT motifs in the Hoxd-4 promoter. This effect is specific in that murine HOXA-1 (HOX-1.6) is unable to activate **transcription** through the Hoxd-4 autoregulatory element. Here we show that this is due to an inability of the HOXA-1 **homeodomain** to bind a HOXD-4 recognition site effectively. We have produced chimeras between

HOXD-4 and HOXA-1 to map specific residues responsible for this functional difference. When positions 2 and 3 in the N-terminal arm of HOXA-1 were converted to HOXD-4 identity, both strong DNA binding and transcriptional activation were rescued. This substitution appears to confer an increased DNA-binding ability on the HOXA-1 **homeodomain**, since we were unable to detect a high-affinity recognition sequence for HOXA-1 in a randomized pool of DNA probes. The contribution of position 3 to DNA binding has been implicated by structural studies, but this is the first report of the importance of position 2 in regulating **homeodomain**-DNA interactions. Additionally, specific **homeodomain** residues that confer major differences in DNA binding and transcriptional activation between Hox gene products have not been previously determined. Identity at these two positions is generally conserved among paralogs but varies between Hox gene subfamilies. As a result, these residues may be important for the regulation of target gene expression by specific Hox products.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
Chimeric Proteins
*DNA-Binding Proteins: CH, chemistry
*Gene Expression Regulation
*Genes, Homeobox
Mice
Molecular Sequence Data
Oligonucleotide Probes: CH, chemistry
Structure-Activity Relationship
Trans-Activation (Genetics)
***Transcription Factors: CH, chemistry**
***Transcription Factors: GE, genetics**

RN 145420-66-2 (HOX4D protein)
CN 0 (**Chimeric Proteins**); 0 (DNA-Binding Proteins); 0 (Oligonucleotide Probes); 0 (**Transcription** Factors)
GEN Hoxd-4; Hoxa-1

L68 ANSWER 38 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS DUPLICATE 6
AN 94:449831 BIOSIS
DN 97462831
TI A **chimeric homeodomain protein** causes self-compatibility and constitutive sexual development in the mushroom Coprinus cinereus.
AU Kues U; Goettgens B; Stratmann P; Richardson W V J; O'Shea S F; Casselton L A
CS Dep. Plant Sci., Univ. Oxford, South Parks Road, Oxford, UK
SO EMBO (European Molecular Biology Organization) Journal 13 (17). 1994. 4054-4059. ISSN: 0261-4189
LA English
PR Biological Abstracts Vol. 098 Iss. 009 Ref. 117143
AB The A mating type genes of the mushroom Coprinus cinereus encode two classes of putative **transcription** factor with distinctive **homeodomain** motifs (HD1 and HD2). A successful mating brings together different allelic forms of these genes and this triggers part of a developmental sequence required for sexual reproduction. In this report we provide evidence that this developmental programme is promoted by a physical interaction between the two classes of **homeodomain** protein. Rare dominant mutations conferring self-compatibility map to the A locus and result in constitutive operation of the A-regulated developmental pathway. Our molecular analysis of one of these mutations shows that it has generated a chimeric gene by in-frame fusion of an HD2 and an HD1 gene. Fusion has overcome the normal incompatibility between two proteins coded by genes of the same A locus and generated a protein that is sufficient to promote development in the absence of any other active A mating type genes. The fusion protein retains most of the HD2 sequence, but

only the C-terminal part of the HD1 protein. It has only the HD2 **homeodomain** motif as a potential DNA binding domain fused to an essential C-terminal region of the HD1 protein, which in a normal HD1-HD2 protein complex may be the major activation domain.
ST RESEARCH ARTICLE; COPRINUS CINEREUS; A MATING TYPE; HD1 **TRANSCRIPTION** FACTOR; HD2 **TRANSCRIPTION** FACTOR; GENE REGULATION; MOLECULAR SEQUENCE DATA; NUCLEOTIDE SEQUENCE; AMINO ACID SEQUENCE
CC Genetics and Cytogenetics-Plant *03504
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics-Molecular Properties and Macromolecules *10506
Metabolism-Nucleic Acids, Purines and Pyrimidines 13014
Developmental Biology-Embryology-Morphogenesis, General 25508
Plant Physiology, Biochemistry and Biophysics-Growth, Differentiation *51510
Plant Physiology, Biochemistry and Biophysics-Reproduction *51512
Plant Physiology, Biochemistry and Biophysics-Metabolism 51519
BC Basidiomycetes 15310

L68 ANSWER 39 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 94:303101 BIOSIS
DN 97316101
TI Fusion with E2A alters the transcriptional properties of the **homeodomain** protein PBX1 in t(1;19) leukemias.
AU Lebrun D P; Cleary M L
CS Lab. Exp. Oncol., Dep. Pathol., Stanford Univ. Med. Cent., Stanford, CA 94305, USA
SO Oncogene 9 (6). 1994. 1641-1647. ISSN: 0950-9232
LA English
PR Biological Abstracts Vol. 098 Iss. 002 Ref. 022613
AB The t(1;19) chromosomal translocation is observed in pre-B cell acute lymphoblastic leukemias and results in expression of **chimeric** E2A-PBX1 **proteins** that contain transcriptional activation domains from E2A and the **homeodomain** of PBX1. Since **homeodomains** mediate DNA-binding, a potential model for the action of E2APBX1 is that it disrupts the transcriptional regulation of genes normally controlled by PBX1 or its closely-related family members PBX2 or PBX3. Using a binding site selection assay, we identified a consensus nucleotide sequence ATCAATCA specifically bound by the PBX1 **homeodomain** and those of its closely-related family members PBX2 and PBX3. An endogenous protein with the properties of PBX3b specifically bound to this sequence in nuclear extracts of precursor B cells. Transfection of reporter genes containing PBX binding sites linked to a minimal promoter demonstrated transactivation by E2A-PBX1 fusion protein dependent upon presence of the **homeodomain**. In contrast, wild-type PBX proteins were incapable of activating **transcription**. The striking differences in transcriptional properties of fusion and wild-type PBX proteins provides strong functional evidence for the importance of aberrant transcriptional regulation in the genesis of t(1;19)-bearing leukemias.
ST RESEARCH ARTICLE; HUMAN; CHROMOSOME TRANSLOCATION; LYMPHOBLASTIC LEUKEMIA; DNA BINDING
CC Genetics and Cytogenetics-Human *03508
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines 10062
Replication, Transcription, Translation *10300
Blood, Blood-Forming Organs and Body Fluids-Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System *15008
Neoplasms and Neoplastic Agents-Blood and Reticuloendothelial Neoplasms *24010
BC Hominidae 86215

L68 ANSWER 40 OF 47 MEDLINE
AN 94376898 MEDLINE
TI Interaction between two **homeodomain** proteins is specified by a short C-terminal tail [published erratum appears in Nature 1994 Nov 17;372(6503):279].
AU Stark M R; Johnson A D
CS Department of Biochemistry and Biophysics, School of Medicine, University of California, San Francisco 94143-0502..
SO NATURE, (1994 Sep 29) 371 (6496) 429-32.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
EM 9412
AB Two yeast **homeodomain** proteins, a1 and alpha 2, interact and cooperatively bind the haploid-specific gene (hsg) operator, resulting in the repression of a set of genes involved in the determination of cell type. The cooperative binding of a1 and alpha 2 to DNA can be reconstituted in vitro using purified fragments of a1 and alpha 2. Only the **homeodomain** is needed for a1, but for alpha 2 a C-terminal 22-amino-acid tail is required as well. As most of the specificity of DNA binding appears to derive from a1, we proposed that alpha 2 functions in the a1/alpha 2 heterodimer to contact a1 with its tail. By construction and analysis of several chimaeric proteins, we investigate how two DNA-binding proteins, one with low intrinsic specificity (alpha 2) and one with no apparent intrinsic DNA-binding ability (a1), can together create a highly specific DNA-binding activity. We show that the 22-amino-acid region of alpha 2 immediately C-terminal to the **homeodomain**, when grafted onto the a1 **homeodomain**, converts a1 to a strong DNA-binding protein. This alpha 2 tail can also be attached to the Drosophila engrailed **homeodomain**, and the chimaeric protein now binds cooperatively to DNA with a1, showing how a simple change can create a new **homeodomain** combination that specifically recognizes a new DNA operator.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Base Sequence
Chimeric Proteins: ME, metabolism
Cloning, Molecular
Drosophila
DNA: CS, chemical synthesis
*DNA: ME, metabolism
*DNA-Binding Proteins: ME, metabolism
Escherichia coli
*Fungal Proteins: ME, metabolism
Helminth Proteins: ME, metabolism
Insect Hormones: ME, metabolism
Molecular Sequence Data
Operator Regions (Genetics)
Protein Binding
Protein Conformation
Transcription Factors: ME, metabolism
RN 122158-15-9 (Unc-86 protein); 146153-32-4 (mec-3 protein); 9007-49-2 (DNA)
CN 0 (activator 1 protein); 0 (alpha2 **homeodomain** protein); 0 (engrail protein, Drosophila); 0 (**transcription** factor Mcm1); 0 (**Chimeric Proteins**); 0 (DNA-Binding Proteins); 0 (Fungal Proteins); 0 (Helminth Proteins); 0 (Insect Hormones); 0 (**Transcription** Factors)
GEN hsg

L68 ANSWER 41 OF 47 MEDLINE
AN 94173687 MEDLINE

TI A proline-rich transcriptional activation domain in murine HOXD-4 (HOX-4.2).
AU Rambaldi I; Kovacs E N; Featherstone M S
CS McGill Cancer Centre, Montreal, Quebec, Canada..
SO NUCLEIC ACIDS RESEARCH, (1994 Feb 11) 22 (3) 376-82.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-J03770
EM 9406
AB The product of the murine Hoxd-4 (Hox-4.2) gene is a **transcription** factor that acts upon an autoregulatory element in Hoxd-4 upstream sequences (1). Using this activity as an assay in transient transfections of P19 embryonal carcinoma (EC) cells, we performed a mutational analysis to map functional domains in the HOXD-4 protein. The importance of the **homeodomain** was shown by a single amino acid change in this region that abolished activity. Deletion analysis revealed that many evolutionarily conserved regions outside of the **homeodomain** were dispensable for activation in our assay. Fusions to the GAL4 DNA-binding domain mapped a transcriptional activation function to the HOXD-4 proline-rich N-terminus. The proline-rich **transcription** factor AP2 squelched activation by HOXD-4 and by GAL4/HOXD-4 N-terminus fusion proteins. Together, these results suggest that HOXD-4 harbors a transcriptional activation domain of the proline-rich type.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
Chimeric Proteins: CH, chemistry
*DNA-Binding Proteins: CH, chemistry
DNA-Binding Proteins: GE, genetics
DNA-Binding Proteins: ME, metabolism
Gene Expression Regulation
*Genes, Homeobox
Mice
Molecular Sequence Data
Mutagenesis, Site-Directed
Proline
Promoter Regions (Genetics)
Structure-Activity Relationship
Trans-Activation (Genetics)
***Transcription Factors: CH, chemistry**
Transcription Factors: GE, genetics
Transcription Factors: ME, metabolism
Transcription, Genetic
RN 145420-66-2 (HOX4D protein); 147-85-3 (Proline)
CN 0 (enhancer-binding protein AP-2); 0 (**Chimeric Proteins**); 0 (DNA-Binding Proteins); 0 (**Transcription** Factors)
GEN Hoxd-4

L68 ANSWER 42 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 93:387956 BIOSIS
DN BA96:63256
TI FUNCTIONAL SPECIFICITY OF THE ANTENNAPEDIA **HOMEODOMAIN**.
AU FURUKUBO-TOKUNAGA K; FLISTER S; GEHRING W J
CS DEP. NEUROBIOLOGY, ZOOLOGISCCHES INST., UNIV. BASEL, RHEINSPRUNG 9, CH-4051 BASEL, SWITZ.
SO PROC NATL ACAD SCI U S A 90 (13). 1993. 6360-6364. CODEN: PNASA6 ISSN: 0027-8424
LA English
AB The segmental identity in animal development is determined by a set

of homeotic selector genes clustered in the invertebrate HOM or vertebrate Hox homeobox complexes. These genes encode proteins with very similar **homeodomains** and highly diverged N- and C-terminal sequences. The Antennapedia (Antp) **homeodomain**, for instance, differs at only five amino acid positions from that of Sex combs reduced (Scr) protein. Using a heat shock assay in which **chimeric** Antp-Scr **proteins** are expressed ectopically in Drosophila, we have shown that the functional specificity of the Antp protein is determined by the four specific amino acids located in the flexible N-terminal arm of the **homeodomain**. The three-dimensional structure of the Antp **homeodomain**-DNA complex shows that this N-terminal arm is located in the minor groove of the DNA, suggesting that the functional specificity is determined either by slight differences in DNA binding and/or by selective interactions with other **transcription** factor(s).

ST DROSOPHILA DNA BINDING **TRANSCRIPTION** FACTOR INTERACTION TRANSCRIPTIONAL GENE REGULATION

CC Genetics and Cytogenetics-Animal *03506
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics-Molecular Properties and Macromolecules *10506
Metabolism-Nucleic Acids, Purines and Pyrimidines 13014
Developmental Biology-Embryology-General and Descriptive 25502
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology *64076

BC Diptera 75314

L68 ANSWER 43 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS

AN 93:387753 BIOSIS

DN BA96:63053

TI ECTOPIC EXPRESSION AND FUNCTION OF THE ANTP AND SCR HOMEOTIC GENES THE N-TERMINUS OF THE **HOMEODOMAIN** IS CRITICAL TO FUNCTIONAL SPECIFICITY.

AU ZENG W; ANDREW D J; MATHIES L; HORNER M A; SCOTT M P

CS DEP. DEV. BIOL. AND GENETICS, STANFORD UNIV. SCH. MED., STANFORD, CA 94305-5427, USA.

SO DEVELOPMENT (CAMB) 118 (2). 1993. 339-352. CODEN: DEVPED ISSN: 0950-1991

LA English

AB The **transcription** factors encoded by homeotic genes determine cell fates during development. Each homeotic protein causes cells to follow a distinct pathway, presumably by differentially regulating downstream 'target' genes. The **homeodomain**, the DNA-binding part of homeotic proteins, is necessary for conferring the specificity of each homeotic protein's action. The two Drosophila homeotic proteins encoded by Antennapedia and Sex combs reduced determine cell fates in the epidermis and internal tissues of the posterior head and thorax. Genes encoding **chimeric** Antp/Scr **proteins** were introduced into flies and their effects on morphology and target gene regulation observed. We find that the N terminus of the **homeodomain** is critical for determining the specific effects of these homeotic proteins in vivo, but other parts of the proteins have some influence as well. The N-terminal part of the **homeodomain** has been observed, in crystal structures and in NMR studies in solution, to contact the minor groove of the DNA. The different effects of Antennapedia and Sex combs reduced proteins in vivo may depend on differences in DNA binding, protein-protein interactions, or both.

ST DROSOPHILA DNA BINDING PROTEIN-PROTEIN INTERACTION ANTENNAPEDIA SEX COMBS REDUCED **TRANSCRIPTION** FACTOR DEVELOPMENT

CC Genetics and Cytogenetics-Animal *03506
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies-Proteins, Peptides and Amino Acids 10064

Replication, Transcription, Translation *11[illegible]
Biophysics-Molecular Properties and Macromolecules 11516
Biophysics-Membrane Phenomena *11518
Developmental Biology-Embryology-Morphogenesis, General *25518
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology *64076
BC Diptera 75314

L68 ANSWER 44 OF 47 MEDLINE
AN 93011007 MEDLINE
TI A POU-A related region dictates DNA **binding** specificity of LFB1/HNF1 by orienting the two XL-**homeodomains** in the dimer.
AU Tomei L; Cortese R; De Francesco R
CS Istituto di Ricerche di Biologia Molecolare P. Angeletti, Roma, Italy.
SO EMBO JOURNAL, (1992 Nov) 11 (11) 4119-29.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9301
AB LFB1/HNF1 regulates the hepatocyte-specific **transcription** of several genes, **binding** as a dimer to cis-acting elements that match the inverted palindrome GTTAATNATTAAC. The DNA **binding** domain of LFB1/HNF1 is characterized by a unique tripartite structure that includes an unusually long **homeodomain** (domain C), a region related to the POU-specific A-box (domain B) and a short N-terminal dimerization domain (domain A). We report that a recombinant peptide corresponding to the isolated **homeodomain** of LFB1/HNF1 **binds** as a monomer to a half-palindrome **binding** site, but shows diminished sequence specificity. Domain B, in addition to the **homeodomain**, is required and sufficient for proper recognition of LFB1/HNF1-responsive sites. A protein consisting of only these latter **two domains** is a monomer in solution, but forms dimers upon DNA **binding**. The protein-protein contacts established within the bound dimer restrain the orientation of the two **homeodomains** with respect to one another, thus contributing in a critical fashion to the recognition of the dyad symmetry-related LFB1/HNF1 sites. The DNA-independent dimerization domain (domain A) is required to increase the affinity of DNA **binding**, but does not influence the dimer geometry.
CT Check Tags: Animal; Comparative Study
Amino Acid Sequence
Base Sequence
Binding Sites
Chimeric Proteins: ME, metabolism
*DNA: ME, metabolism
DNA-Binding Proteins: GE, genetics
***DNA-Binding Proteins: ME, metabolism**
Escherichia coli: GE, genetics
*Genes, Homeobox
Kinetics
Liver: PH, physiology
Macromolecular Systems
Mathematics
Molecular Sequence Data
Mutagenesis, Site-Directed
Oligodeoxyribonucleotides
Plasmids
Restriction Mapping
Substrate Specificity

Transcription Factors: GE, genetics
***Transcription Factors: ME, metabolism**
Transcription, Genetic
Translation, Genetic
RN **126548-29-6 (liver-specific transcription factor LF-B1)**; 9007-49-2 DNA
CN 0 (**Chimeric Proteins**); 0 DNA-**Binding** Proteins ; 0 (Macromolecular Systems); 0 (Oligodeoxyribonucleotides ; 0 Plasmids ; 0 **Transcription** Factors)

L69 ANSWER 45 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 92:142336 BIOSIS
DN BA93:74561
TI THE OCT-1 POU DOMAIN MEDIATES INTERACTIONS BETWEEN OCT-1 AND OTHER POU PROTEINS.
AU VERRIJZER C P; VAN OOSTERHOUT J A W M; VAN DER VLIET P C
CS LABORATORY PHYSIOLOGICAL CHEMISTRY, UNIVERSITY UTRECHT, VONDELLAAN 24A, 3521 GG UTRECHT, NETH.
SO MOL CELL BIOL 12 (2). 1992. 542-551. CODEN: MCEBD4 ISSN: 0270-7306
LA English.
AB The POU domain is the conserved DNA binding domain of a family of gene regulatory proteins. It consists of a POU-specific domain and a POU **homeodomain**, connected by a variable linker region. Oct-1 is a ubiquitously expressed POU domain **transcription** factor. It binds to the canonical octamer sequence (ATGCAAAT) as a monomer. Here we show by chemical cross-linking and protein affinity chromatography that the Oct-1 POU domain monomers can interact in solution. This association requires both the POU **homeodomain** and the POU-specific domain. The interaction is transient in solution and can be stablized by binding to the heptamer-octamer sequence in the immunoglobulin heavy-chain promoter. This correlates with cooperative DNA binding to this site. POU proteins from different subclasses, including Oct-1, Oct-2A, Oct-6, and a **chimeric** Oct-1 **protein** containing the Pit-1 POU domain, can bind cooperatively to a double binding site and form an heteomeric complex.
ST GENE REGULATORY PROTEIN DNA BINDING DOMAIN **TRANSCRIPTION** FACTOR MOLECULAR SEQUENCE DATA NUCLEOTIDE SEQUENCE
CC Cytology and Cytochemistry-Animal *02506
Genetics and Cytogenetics-Animal *03506
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics-Molecular Properties and Macromolecules *10506

L68 ANSWER 46 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS DUPLICATE 7
AN 93:117506 BIOSIS
DN BA95:61606
TI POU-SPECIFIC **DOMAIN** OF OCT-**2** FACTOR CONFERS OCTAMER MOTIF DNA **BINDING** SPECIFICITY ON HETEROLOGOUS ANTENNAPEDIA **HOMEODOMAIN**.
AU BRUGNERA E; XU L; SCHAFFNER W; APOSTOLI D N
CS INST. MOLECULAR BIOL. II, UNIV. ZURICH, WINTERTHURERSTRASSE 190, CH-8057 ZURICH, SWITZERLAND.
SO FEBS (FED EUR BIOCHEM SOC) LETT 314 (3). 1992. 361-365. CODEN: FEBLAL ISSN: 0014-5793
LA English.
AB The bipartite DNA **binding** domain of the POU family of **transcription** factors contains a 'POU-specific' domain unique to this class of factors and a 'POU **homeodomain**' homologous to other **homeodomains**. We compared DNA **binding** of the Oct-**2** factor POU **domain** and the Antennapedia (Antp) **homeodomain** with a **chimeric** Oct-2/Antp **protein** in which the distantly related Antp

homeodomain was substituted for the Oct-1 POU **homeodomain**. The Oct-2/Antp **chimeric protein** bound both the octamer and the Antp sites efficiently, indicating that DNA **binding** specificity is contributed by both components of the POU domain.

ST DROSOPHILA TRANSCRIPTIONAL GENE REGULATION MOLECULAR SEQUENCE DATA NUCLEOTIDE SEQUENCE

CC Genetics and Cytogenetics-Animal *03506
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics-Molecular Properties and Macromolecules *10506
Metabolism-Nucleic Acids, Purines and Pyrimidines 13014
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology *64076

BC Diptera 75314

L68 ANSWER 47 OF 47 BIOSIS COPYRIGHT 1997 BIOSIS
AN 90:47730 BIOSIS
DN BA89:25094
TI A **HOMEODOMAIN** SUBSTITUTION CHANGES THE REGULATORY SPECIFICITY OF THE DEFORMED PROTEIN IN DROSOPHILA EMBRYOS.
AU KUZIORA M A; MCGINNIS W
CS DEP. MOL. BIOPHYS. BIOCHEM., YALE UNIV., NEW HAVEN, CONN. 06511, USA.
SO CELL 59 (3). 1989. 563-572. CODEN: CELLB5 ISSN: 0092-8674
LA English
AB **Homeodomain** proteins are believed to direct developmental pathways during Drosophila embryogenesis by the specific regulation of other genes. An unresolved issue is whether it is the **homeodomain** or the other regions of such proteins that confer target specificity. To test the role of the homoeodomain in determining target specificity, we replaced the homeobox of Deformed with the homeobox of Ultrabithorax. The resulting **chimeric protein** cannot activate **transcription** from the Deformed gene, as does the normal Deformed **protein**. Instead, the **chimeric protein** activates ectopic **transcription** of Antennapedia, a gene normally regulated by Ultrabithorax. Our results indicate that in the context of the developing embryo, even closely related **homeodomain** sequences have different target specificities.

ST ANTENNAPEDIA GENE ULTRABITHORAX GENE EMBRYO DEVELOPMENT **TRANSCRIPTION**

CC Genetics and Cytogenetics-Animal *03506
Biochemical Studies-Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics-Molecular Properties and Macromolecules *10506
Metabolism-Nucleic Acids, Purines and Pyrimidines *13014
Developmental Biology-Embryology-General and Descriptive *25502
Developmental Biology-Embryology-Morphogenesis, General *25508
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology *64076

BC Diptera 75314